UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY
CIVIL ACTION NO 16-MD-2738(FLW)(LHG)

IN RE JOHNSON & JOHNSON POWDER PRODUCTS MARKETING, SALES PRACTICES.	:	DAUBERT HEARING JULY 25, 2019 VOLUME 4

CLARKSON S. FISHER UNITED STATES COURTHOUSE
402 EAST STATE STREET, TRENTON, NJ 08608

B E F O R E: THE HONORABLE FREDA L. WOLFSON, USDJ

A P P E A R A N C E S:

BEASLEY ALLEN, ESQUIRES
BY: P. LEIGH O'DELL, ESQUIRE (ALABAMA)
-and-
ASHCRAFT & GEREL, ESQUIRES
BY: MICHELLE A. PARFITT, ESQUIRE (VIRGINIA)
-and-
LEVIN PAPANTONIO, ESQUIRES
BY: CHRISTOPHER V. TISI, ESQUIRE (FLORIDA)
-and-
ROBINSON CALCAGNIE, ESQUIRES
BY: CYNTHIA L. GARBER, ESQUIRE (CALIFORNIA)
behalf of the Plaintiffs Steering Committee

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On behalf of Defendant Johnson & Johnson

(Continued)

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A P P E A R A N C E S C O N T I N U E D:

WEIL GOTSHAL & MANGES, ESQUIRES
BY: ALLISON M. BROWN, ESQUIRE
On behalf of Defendant Johnson & Johnson

SEYFARRTH & SHAW, ESQUIRES
BY: THOMAS L. LOCKE, ESQUIRE (WASHINGTON D.C.)
On Behalf of Defendant Personal Care Products Council

M O R N I N G S E S S I O N

(In open court.)

THE DEPUTY CLERK: All rise.

THE COURT: Thank you. Everyone may be seated.

MS. PARFITT: At this time Plaintiffs will call Dr. Anne McTiernan.

ANNE MC TIERNAN, called as a witness on behalf of the Plaintiffs, having been first duly sworn, testified as follows:

DIRECT EXAMINATION

BY MS. PARFITT:

Q. Dr. McTiernan, good morning.

A. Good morning.

Q. Would you please introduce yourself to the Court.

A. Good morning, your Honor. My name is Dr. Anne McTiernan.

Q. Dr. McTiernan, have you brought with you today, for purposes of assisting you with the opinions you will be sharing with her Honor your expert report and your curriculum vitae and addendum tables?

A. Yes.
Q. Have you also brought with you a binder of materials that consist of the relevant literature you may be discussing this morning with the Court?
A. Yes.
Q. Finally, in preparation for your testimony today, did you assist me in preparing some slides that we can focus on today?
A. Yes.
Q. We will be showing those throughout the course of the morning.

Dr. McTiernan, would you share with us what your profession and field of expertise is.
A. I'm an epidemiologist, and I specialize in women's health and cancer epidemiology.
Q. We need to hear what epidemiology is, and frankly why the field of epidemiology is important for the discussion this morning of ovarian cancer and talcum powder.
A. Epidemiology is the study of disease in humans, disease and risks. In epidemiology, we can determine what are the associations between an exposure and risk of disease. This is critical for this issue of talcum powder products use in ovarian cancer because we don't have clinical trial evidence. Studies in humans we're

really relying on epidemiology.

Q. You may move just a little bit closer to the mic. Thank you.

Dr. McTiernan, if you will, summarize for the Court -- and we will put a slide up here -- your qualifications and expertise to prepare you to offer the opinions you will be giving in this case.

A. In 1982 I completed a Ph.D. in epidemiology at the University of Washington in Seattle, and I focused on cancer epidemiology.

In 1989, I completed my medical degree at New York Medical College. And then I moved to Seattle and completed a residency in internal medicine at the University of Washington in 1992.

Q. If you will -- we will move to the next slide -- briefly summarize for the Court the qualifications and expertise with regard to academic appointments and research.

A. Sure.

I am a full member at the Fred Hutchinson Cancer Research Center in Seattle. This is a premier independent cancer research center that first identified bone marrow transplant, and it was the first cancer prevention center in the country. There I study ways to prevent new and recurrent cancer. I

conduct epidemiologic research, identify risk factors for women such as breast and ovarian cancer, and I study prevention methods to reduce population and other markers of cancer risk.

I am also a research professor at the University of Washington Schools of Medicine And Public Health, and my departments there are epidemiology and gerontology and geriatric medicine. There I teach and mentor epidemiology students, especially graduate students.

Q. What other research activities are you involved in?

A. One key one is the Women's Health Initiative. When I began at Fred Hutchinson in 1992, I was hired to be a project director for the Women's Health Initiative. This includes a cohort study that we will be talking about later.

Q. If I can ask a question here. You are speaking of the Women's Health Initiative also the Houghton Study?

A. That's correct.

Q. You were project director?

A. Yes.

Q. Please.

A. There I've led the development of protocols

procedures, recruitment interventions because we had trials as well, follow-up and outcomes including ovarian cancer.

In terms of published research, I have published over 400 scientific manuscripts and peer-reviewed medical and scientific journals.

We put up here numbers of different types of studies we will be talking about later that I've published. I've published 17 case-control studies, 127 cohort studies, 165 randomized clinical trials, ten pooled analyses, five methods, multiple meta-analyses and multiple reviews.

Q. Thank you. We will be speaking about many of those a bit later.

Now, will you briefly discuss with us positions where you are in an advisory or consultancy position for either a national or international research organization?

A. Sure. Two relevant ones are for the World Health Organization. They are the International Agency for research on cancer. This is the cancer branch of the World Health Organization.

In 2002 I was a member of a working group that completed a systematic review and produced a handbook of cancer prevention. That one was focused on

physical activity and weight control. There I chaired a section to identify biologically plausible mechanisms linking physical activity and weight to cancer.

Q. Now, if you will, in the interest of time, just briefly share with us as well what your work has been with the World Cancer and other groups.

A. The World Cancer Research Fund, I'm a member of the Continuous Update Panel that conducts research on cancer prevention and survivorship, and this is focused on diet, nutrition, physical activity, and obesity.

Q. The work you do for the World Cancer Research Fund is just focused on certain research areas?

A. That's correct, diet, nutrition, physical activity and obesity.

Q. Please, if you will.

A. I also advised for the U.S. Government, which includes advisory for the U.S. Department of Health and Human Services advisory committees on physical activity guidelines in 2008 and 2018, and there I was chair of the cancer subcommittee.

I have been principal investigator of multiple NCI grants, including the Seattle Transdisciplinary Research on energetics and cancer.

I have been a program reviewer for NCI research and reviewed grant applications.

I have also reviewed grant applications for the Department of Defense.

Q. Dr. McTiernan, you spoke briefly about the numerous almost 400 publications that you have prepared over the course of your career. Do you also act as a peer reviewer?

A. Yes. For many medical and scientific journals. It has been an ongoing work that I do.

MS. PARFITT: Your Honor has your resume. We are going to move forward and address some of the other issues, if I may.

THE WITNESS: Okay.

Q. Dr. McTiernan, what was the issue you were asked to review in this case?

A. So I was retained to review the current state of the scientific literature regarding talcum powder products and to opine on whether these products cause ovarian cancer.

Q. Have you formulated an opinion regarding the association between talcum powder products and ovarian cancer, and are you prepared today to share your methodology for developing those opinions?

A. Yes.

Q. What are those opinions?
A. My opinion as an epidemiologist and physician, stated to a reasonable degree of medical and scientific certainty, that use of talcum powder products, including Johnson & Johnson Baby Powder and Shower To Shower, in the genital perineal area can cause ovarian cancer. I base this opinion on the statistically significant elevated risk seen with the epidemiology data when they are combined, the pathological evidence, the consistency of results across geographic areas, and in different race and ethnic groups, evidence of a positive dose-response effect, and the plausible biological mechanism.
Q. Dr. McTiernan, have you ever testified in a court of law as an expert witness?
A. No, I have not.
Q. This is your first time in almost forty years of a practicing epidemiologist that you have had the pleasure of sitting up there and being quizzed. Is that correct?
A. Yes.
Q. Dr. McTiernan, why did you decide to be an expert witness in this case?
A. First I thought it would be an important issue in women's health and public health. Second, I wanted

to share my scientific skills and expertise on this issue.

Q. Now, in addition to your opinions you have set forth in this litigation as an expert, have you shared your opinions outside of this litigation?

A. Yes, I have.

Q. To whom have you shared your opinions?

A. There are two major areas where I have shared publicly. The first is with Health Canada. Health Canada prepared and released a document publicly and that stated that the meta-analyses of available human study in the peer-reviewed literature indicated consistent and statistically significant positive association between perineal exposure to talc and ovarian cancer, and they stated further that available data are indicative of a causal effect. This conclusion agrees with my own, and that's what I stated to them in public commentary.

Q. We'll get to the public commentary in just one moment.

A couple of questions. To your understanding, were there any dissimilarities between your conclusions or your findings and that of Health Canada?

A. They were quite similar. One difference is they

made the assumption there was no asbestos in the talcum powder products.

Q. For purposes of your opinions that you are sharing not only with the Court but the Health Canada and Congress, you understand there is a presence of asbestos as well?

A. Yes.

Q. Did you both do a systematic review?

A. I did.

Q. Did you both do a Bradford Hill causality analysis?

A. Yes.

Q. You started to mention about a commentary. Were you provided an opportunity, after your read of the Health Canada assessment, to provide your remarks to Health Canada or your opinions to Health Canada?

A. Yes.

Q. You did that?

A. Yes.

Q. Why don't you tell us when and what you did.

A. So in February of 2019, I submitted comments to their website. They invited public commentary.

Q. What is it that you shared with Health Canada?

A. I stated their conclusion agreed with mine. I told them how many publications I had reviewed, and

including pooled and meta-analyses, and I stated the meta-analysis consistently showed that women who had ever used talcum powder products in the genital area had a statistically significant 22 to 31 percent increased risk of developing epithelial ovarian cancer overall, compared with women who had never used these products. I stated that the comprehensive combined analyses also showed strong evidence of increased risk of ovarian cancer with increasing number of lifetime applications of these products in the perineal/genital area.

Q. After you submitted your comments, Dr. McTiernan, what, if any, response did you receive from Health Canada?

A. The next slide shows their acting senior manager contacted me and asked if I would be willing to offer my scientific opinion and my expertise to help them as they conclude their project.

Q. Dr. McTiernan, after you made your comments public to Health Canada and received a response by the authorities at Health Canada requesting your expertise in the future, did you have an opportunity to share the opinions you are expressing today in the courtroom with anyone else? I believe you mentioned Congress?

A. Yes, I did.

Q. Tell us about that.
A. I gave testimony to the U.S. Congress, to their Committee on Oversight and Reform, Subcommittee on Economic and Consumer Policy.
Q. And, specifically, how did that come to be? What were you asked to do so you knew what your responsibility or role would be before Congress?
A. One week before this meeting I was contacted by the Committee and asked to provide my comments on the association between talcum powder product use and risk of ovarian cancer.
Q. And did you have to submit that public comment?
A. I did. I had a prepared five minutes of the comments, and I also had the opportunity to submit a document, and those are public.
Q. What I would like you to do is share with Her Honor what your comments were to Congress with regard to your opinions with regard to genital use of talcum powder and causing ovarian cancer. What did you tell Congress?
A. I told them how many studies I had reviewed. I told them that summarizing the data across those studies consistently showed women who had ever used these products in the genital area had a statistically significant 22 to 31 percent increased risk of

developing epithelial ovarian cancer compared with women who never used them.

I further talked about the combined analysis that showed increasing amount of exposure to these products, increased risk of developing ovarian cancer further, and this is dose-response. We'll talk more about that later.

Q. Next slide.

What else did you share with Congress?

A. I further talked about biologically plausible pathways through which these products can be causing ovarian cancer and a particular focus on inflammatory response that is caused by talc.

Also I talked about, given the frequency with which asbestos has been found in personal use talc products, I reviewed the literature on the epidemiology of asbestos and risk of ovarian cancers.

And then I informed them that in 2012, the International Agency for Research on Cancer stated that a causal association between exposure to asbestos and cancer of the ovary was clearly established, and that that agency had classified fibrous talc, a component of talcum powder products, as a Class 1 carcinogen, the most dangerous level of carcinogen.

Q. Dr. McTiernan, so within this last year, you

have shared your published opinion on two occasions: Health Canada and Congress. Is that correct?

A. Correct.

Q. What I would like to do now, Dr. McTiernan, is to move on to the methodology.

Her Honor is interested in hearing what the methodology was and is that you employed in order to arrive at your opinions that talcum powder products can cause ovarian cancer.

Why don't we pull up the next slide.

What I'll ask you to do is walk the Court through your methodology in a systematic way using the chart, if that is helpful.

A. Okay.

As I would do for any scientific research of this type, what I am trying to look at, an overview and do causal assessments, I would first formulate a question. So I did that.

The question in this case is: What is the association between talcum powder products and ovarian cancer?

The second question was: Can the use of talcum powder products cause ovarian cancer?

I've conducted a systematic review --

Q. When you say "systematic review," we heard about

systematic reviews. What is it?
A. It means you make the effort to look at all available evidence -- in this case, epidemiologic evidence, and that you do a careful searching through a database and through relevant journal articles to make sure you have the totality.

To do that, I defined search terms for the database. I conducted a PubMed search. I provided inclusion and exclusion criteria. From all of that, after reviewing all that, I found -- I identified 38 relevant original and peer-reviewed epidemiologic publications.

As I continued my work on the report, I updated the search and I continued to do that.
Q. What is the next step?
A. The next step is reviewing the data. So I reviewed relevant epidemiologic studies. In those studies I considered the statistical data, the strength and weaknesses of study type, the effect of possible bias, chance, confounding and differences in exposure measures. I considered dose-response, what we talked about before. I also considered data from non-epidemiologic lines of evidence, such as animal, cell, clinical and pathological studies. I considered non-talc components of talcum powder products and

impact on carcinogenicity such as asbestos, fibrous talc, heavy metals, and fragrances.

Q. After you had gathered this body of evidence, it included not only epidemiologic evidence but also other sciences that speak to the biological plausibility that speak to cellular studies, animal studies, pathological studies, you moved on to try to aggregate it. Is that correct?

A. Yes.

Q. Please.

A. I extracted data into four tables. We provided those. In my report there is Table H for case-control, cohort, meta-analyses and pooled studies.

Q. Putting those tables together that are at the end of your expert report, how did you go about extracting certain study characteristics and why did you do that?

A. I chose the study characteristics that would be most important to know about the breadth and depth of individual studies, particularly to be able to know how large the study was, where it was conducted, when it was conducted, how many cases were included, how many people without cancer were included, if it was a cohort, how long it had been followed. I looked at

dose-response. The key metric is relative risk. Relative risk is clearly the important element. And I also looked at the statistical testing on cancer subtype.

Q. One follow-up. Why was it important, relevant to the study of science that you extract this kind of information from the studies?

A. It is relevant in interpreting their final results because these elements influence the results they get and what they might mean.

Q. Thank you.

Then what did you do?

A. Then I conducted what we call a Bradford Hill analysis; and using this analysis, which is a way to assess for causality, I used independent judgment, I weighed relevant evidence, and reached a conclusion.

Q. Thank you, Dr. McTiernan.

Dr. McTiernan, is the epidemiology you have employed in this case for purposes of developing your opinions recognized and generally accepted by those scientists in your field of expertise?

A. It is, yes.

Q. Do you in your own research and academic work employ these same types of scientific reasoning and epidemiology that you have used for purposes of

developing your opinions in this case?
A. I do. Most recently and notably the U.S. Government work I have done for the physical activity guidelines we used a similar process to evaluate literature and do causal analysis and determine what we believe the literature is stating.
Q. In the course of talking about the methodology that you employed in order to arrive at the opinions that you have shared and will continue to share with us today and have publicly, you talked about certain epidemiological designs. We're going to have a little teaching session, if you will.

To the extent you can tie in any of your thoughts your opinions with regard to talcum powder, you can use those as examples. What I would like to do is take the next probably five, ten minutes just to get a basic understanding of how you are going to be approaching the studies for the Court and explaining what they actually mean. All right?
A. Okay.
Q. Let's step back and talk about the four different types of study designs.
A. The four types of data that are available for this issue -- ovarian cancer and talcum powder product use.

The first is case-control studies. This is where investigators would identify individuals with ovarian cancer and then would identify people without cancer, interview both about their use of products and other variables to help with the interpretation, and then they compare what exposure did the cases have and what exposure did the controls have.

Q. In this case, exposure to talcum powder products?

A. Yes.

Q. In this case, what disease?

A. Ovarian cancer.

Q. Go ahead.

A. Modern case-control studies tend to be population-based. The reason for that is to be generalizability. So if you have results from a case-control study, can that refer to what the most likely universe of results would be?

Q. Let's step back a little bit.

There are two different types of case-control studies.

A. Yes, the first is population based.

Q. What does that mean?

A. It means the cases and controls come from the population. The cases often are identified through a

registry, and the controls will be from some population group.

A second type of case-control studies is hospital-based, and that's where investigators in one hospital identify all the cases of ovarian cancer that have happened in some period of time.

The controls they would select from other hospitalized patients that don't have ovarian cancer. This type of case-control study is less likely to be done.

Q. Which one?

A. Hospital-based, because you can't generalize it to the general population. And because the controls who are sick and in the hospital may be sick for different reasons than the cases.

So, ideally, in a case-control study, the cases and controls would be very similar except for the one exposure you want to look at in this case, talcum powder products. We want to get rid of all of the other kind of noise you could have when you are looking at real people.

The second kind of study is a cohort study. This is a study where women are identified at one point, invited into a long-term prospective study. They complete forms when they enter the study,

questionnaires; and, in this case, all of those studies were self-administered questionnaires.

Q. What is a "self-administered questionnaire"?

A. As it sounds, the person completes the form themselves. Case-control studies, usually the data are collected through an interviewer, a trained interviewer. So in the cohort studies, the women enter -- the cohort, they complete the forms, datas are collected and they are followed up over time until cancers occur -- in this case, ovarian cancer, because ovarian cancer is rare, you need a couple of hundred thousand women followed for 20 years to find a large number of cancer cases.

Q. When you say "cases," there is a difference between the total population that enters the study and those actual cases of cancer?

A. Yes. The critical number is the number of cases. I have been involved with the design of several cohorts and you design your cohort to be a certain size in order to have the right number of cases developing. It is the number of cases of ovarian cancer that occur. That's the key variable.

Q. Is there also another type of study where we aggregate information?

A. Yes. There are two, and one is called

meta-analysis. This is where an investigator collects data from published studies. So they get the specific statistics from a published study and then analyzes them and combines them into one summary statistic. They collect this number called relative risk from different studies and they combine those relative risks so they could have one relative risk. It gives you a very big summary of what the literature looks like overall.

Q. We'll be talking about those a bit later.

What is the next study?

A. The next study is a pooled analysis. This is where individual level data are obtained from the individuals in the study, in this case, women. So women with ovarian cancer, women without ovarian cancer. Their data then are analyzed as if it is one large study, and we have then also summary statistics that are developed. It is a very excellent way of looking at data overall.

Q. The value of doing an aggregate type of combined study like meta-analyses and pooled would be what?

A. You really can see what the picture is overall. You can have much larger numbers. The pooled example, the pooled study we'll talk about has 14,000 cases in it. So you really have enough numbers to see what's

going on. You could look at subgroup analyses. You could look at dose-response. There is a lot of advantages to looking at pooled analyses.

Q. We'll talk about that a little bit later.

Dr. McTiernan, we talked about these observational types of studies. Correct?

A. Yes.

Q. Is there any type of study you do use in your academic and professional research world and considered but did not utilize in this case?

A. Yes. I conduct randomized clinical trials for many different purposes. The Women's Health Initiative had three randomized trials in it. In this case, first, if you did a randomized clinical trial to test where the talcum powder products cause ovarian cancer, first of all, you would need hundreds of thousands of women followed for decades before you would have enough ovarian cancer cases developing. Much more importantly, it would be the ethics, it would not be ethical to test in a randomized trial something you think could be harmful in order to see if it does cause harm. So randomized trials always have to have the goal of can something have a benefit.

Q. Thank you. Dr. McTiernan, in your professional research and academic work, do you design and publish

all core types of those studies, including randomized control trials?

A. I do, yes.

Q. In evaluating the totality of the epidemiological data on talcum powder products and ovarian cancer, did you invoke a hierarchy of evidence in order to better examine the association, the relationship between talcum powder and ovarian cancer?

A. No, I did not. I looked at the totality. I looked at all of the studies, and I looked at the studies that combined information. I looked at everything.

Q. I guess, my question is you have this choice of five studies. You talked about why you didn't look at any randomized control trials. But with regard to the case-control, the cohort, the meta-analyses, and the pooled study, are there reasons that one type of study might be more reliable, specifically when you are looking at the issues you were asked to look at here?

A. All of those studies provide useful information. So I considered all of them. I did not place any hierarchy on them. They all give useful information.

Epidemiology studies all can have benefits, strengths, and they can all have weaknesses. I considered all of that when I reviewed the data.

Q. The defendants here, you read their briefing and suggested you should have made your focus more on the cohort studies rather than you case-control studies. Do you recall reading that?
A. I do.
Q. Why don't you agree with that?
A. There are benefits and drawbacks to all these types of studies. I do not believe for this particular question when you are looking at what a woman has used, and you want to know her lifetime exposure, and you want details, you are going to see that best described in a case-control study that can be focused. The cohort studies have their strengths, and we'll go over those in a bit also. I found both types of studies provided useful information, and I summarized that in my deliberations.
Q. In your work as a professional and researcher, is there an example wherein a particular study type was more suited for a particular scientific question?
A. There are some instances, and I can give one example. With the World Cancer Research Fund, I sit on a panel that advises them on interpretation of dietary data. Their mission is to focus on diet, and diet is a very interesting thing to try to collect, because if you ask people about their diet and they

have already developed cancer -- so in a case-control study you will be asking people with cancer about their diet, and comparing them to controls without the diet. Once somebody develops cancer, their diet changes dramatically. If you want to know what somebody's previous diet effect on cancer risk is, it is very difficult to do that in a case-control study. The person has already changed. Diet, you can't ask somebody what they have eaten in the past. We've tried but researchers found that diet, if you ask somebody at one point what the diet was a year ago, they will tell you what they are currently eating, even though they think it is a year ago, and this has been tested. Diet is one very particular study, a variable. It is complicated. It is not like you are asking somebody how many eggs you ate. The dietary forms in the Women's Health Initiative had 150 items, and for each item you are asking people how often they eat it and how large a serving is. You can imagine how complicated that is, and then if you ask somebody to recall that.

So for diet studies, it is really an example of somewhere where a cohort study may be more helpful; ask somebody when they enter the cohort study what their complicated dietary pattern was, and then follow

them forward over time. You still have the issue where you need to have a huge study to follow and follow them long enough until ovarian cancer develops.

Q. Johnson & Johnson claims your reliance on study science in the case of talcum powder products and ovarian cancer is inconsistent with the work you did with the World Cancer Research Fund, which was involving dietary habits and the need to do at that time a cohort study. Is the work you have done in this case inconsistent with your prior research in epidemiology?

A. It is not inconsistent with my overall research of published 17-case-control studies. I have been principal investigator of a case-control study. I participated in a pooled analysis involving my data from case-control studies. I participated in even more cohort studies. Hundreds of publications have come out from the cohort studies that I worked with. So I've looked at studies -- I've used studies across the board in epidemiology because sometimes one study works better than another. Sometimes you do both.

Q. And it depends on the study question. Is that correct, Dr. McTiernan?

A. Absolutely, yes.

Q. I'm going to shift gears a little bit now and

talk a little bit now, if you will, ask you to talk about the first group of studies, and that would be -- you talked about some tables you put together. Is that right?

A. Yes, for the expert report.

THE COURT: Those tables did not come out on my copy.

MS. PARFITT: We're not going to be using those at all. It is a question.

Q. The reason for that demonstrative, Dr. McTiernan, is just so you could identify for the Court that there were four tables that you put together?

A. Yes, they are.

Q. And they dealt with data you selected from the four different study types we just talked about. Correct?

A. Yes.

Q. Did you assist me in taking that data and putting that data together in four plots for the individual studies?

A. Yes. You assisted me. I told you what I needed and then you kindly did the forest plot part for me, yes.

Q. We're going to get to those in just a moment.

Why did you want a forest plot. What was the

purpose of plotting it along a forest plot?
A. A forest plot is a way to visualize what's happening across studies. It is a commonly used method. If you look at the meta-analysis, trying to see what did the data look like across studies, they will do this, forest plot.
Q. Directing your attention to this next exhibit, it is a case-control and cohort study, all ovarian, 1982 to 2016. Would you share with us the information that's contained, perhaps giving us, first, a description of the types of information and, then, we're going to talk about how you interpreted that. Fair?
A. Okay. I'm going to mark on the PowerPoint what I'm pointing at.

This table on this side has the data that I put into my expert report and we put into this slide.

The first column is just the Case-Control Study. That's the name of the study and the year it was published.
Q. How many of those did you review?
A. 28 case control studies. And then the nationality where it was conducted, the numbers of cases. It is a key number to help us interpret these results, how many cases there were.

Q. Does that represent cases of ovarian cancer?
A. Cases of ovarian cancer, yes.

The number of controls, individuals without cancer, whether the study was population-based or hospital-based.

The next column says "DR" and that stands for dose-response. The question was, Did that study address dose-responses? Did the risk increase with increasing doses? If they did address it, that would be "yes"; if they addressed it and found a positive response. If they addressed it and found no dose-response, I would put the word "no" in there. If they did not even attempt it we put N/A. And "incomplete" if they attempted it but they had incomplete data -- we'll talk more about dose-response later.

The next column is "relative risk." Relative risk is the most important statistic in all of these studies. It refers to what is the risk in exposed individuals compared to somebody who is not exposed. What is the risk in somebody who used talcum powder products compared to somebody who did not. So the relative risk tells us the strength, how large was the association. It tells us consistency when we look across different studies. It's the effect size. It

is also called the "point estimate." In some studies you could see the words "odds ratio" or "O.R.". It is the same thing estimating "relative risk."

"HR" stands for "hazard ratio." That means the same thing. So I'm always going to say relative risk here for simplicity.

The next column and the one following it referred to the confidence intervals, the lower limit and upper limit of confidence interval.

Q. Share with us what that means and how it is interpreted.

A. The confidence interval in epidemiologic studies is a statistical tool to see how likely the universe of results would fall within a particular interval. If we knew the universe of results. We don't. So we are always estimating. The confidence interval does not affect what the actual relative risk is for that study. It is just an estimate how the truth might lie if we knew everything.

Q. You said the confidence interval does not affect at the relative risk. Explain that?

A. If you have a small narrow confidence interval, if you have a wide one, if it crosses one, none of that is going to affect what the actual relative risk says. The relative risk always says risk in talcum

powder use versus risk without. That's a key comparison. The confidence interval is a statistical tool that helps us interpret. Confidence intervals can range widely. They will always be around the relative risk.

Q. Can you give us an example.

A. Look at the top one. That studies relative risk. It was approximately 1.4. I should explain. Along the very bottom here we have numbers that refer to a number, that's a relative risk. A risk of one is no effect, no association. If it is a relative risk of 1.2, that would be a 20 percent increased risk for users versus nonusers. If it is to the left of the line, it would be a lower risk in users versus nonusers. If the confidence interval crosses 1, so if it includes one --

Q. Take an example where it crosses 1.

A. You can see right here it's called Moorman. That study's relative risk was to the right of the line. It was a positive relative risk. But the confidence interval crossed the line, so it suggests in the universe the relative risk can fall below 1. It could be a negative risk or it could increase risk because the line also goes to the right.

Q. A situation or study like that where the

confidence interval, the lower bound is below 1, the upper bound is above 1, you now said crossed 1. Is that correct?

A. Yes.

Q. What does that do to the significance of the relative risk, the relative risk is above 1?

A. It doesn't change the relative risk at all. It tells you in the universe, if you knew every person who had ovarian cancer or not, you would have a 95 percent chance of it falling somewhere in that line in that confidence area. It is an estimate where a relative risk might lie.

Q. Is that reliable information, information that scientists should recognize and consider in their evaluation of studies?

A. It is useful, yes. The statisticians tell us not to use it to determine if there is an effect or not or what the effect size is. They tell us it is always the relative risk, and that's how I have interpreted it.

People use this -- many scientists use this term "statistical significance." Statistical significance wasn't invented by statisticians who invented the tools. It was more people that apply it, and some people will say that a study is not

statistically significant if the confidence interval includes one if it extends across that line.

Q. Dr. McTiernan, does a nonsignificant relative risk, meaning that the confidence interval is less than 1, mean that there is no association between the exposure, in this case talcum powder products, and the outcome ovarian cancer?

A. It does not. The association is driven by the relative risk. The confidence interval tells you how likely, if you did know everything, that the relative risk would fall within that confidence interval. That's why it is called confidence interval -- how confident you could be that's where it would fall if you knew the totality of evidence.

The one thing -- there are two things that determine what the confidence interval is. One is how large the sample size is. Large sample size is always better because it gives you more precision. You are more confident your relative risk falls within the confidence interval. Confidence intervals tend to be smaller in the very larger studies.

The other thing that drives it is variability around the average measure.

Q. What do you mean by that?

A. How variable were the numbers; was there a lot

of noise in the data. And so much of that is driven by sample size again, and some of it is driven just by the nature of the data.

I've looked at thousands of forest plots in my daily work. I look at them all the time. It is unusual for a forest plot to show this distribution when most things are to the right of the line --

Q. Can you show us again?

A. -- to the right of 1.0. This tells us we have quite a bit of consistency across the studies.

Q. Is that to the right of the line?

A. To the right of the line.

Most of the studies, almost all, except for two studies, each of those dots refer to a study with a couple of exceptions, almost all those dots, each dot refers to the relative risk, and almost all of them and to the right of the line with two studies exception, one case-control study and one cohort study. There are a couple of studies that are referred to twice here because they provided their data separately for subgroups.

For example, Moorman was a study in white women and black women and that presented the data separately. We couldn't combine it. Booth presented data separately for daily and weekly use, and there

wasn't a way to combine them.

Q. Dr. McTiernan, you were talking about the case-control. Below that dark black line we have some other studies.

A. I was just about to get to that. The cohort studies we put separately because some of the data is a little bit different. In the cohort study, we put the name, the nationality, the number of the cases -- again, a key variable. And the next column says "noncases." These were women in the cohort who did not develop ovarian cancer.

The following column is the follow-up years.

The next column -- the next few columns are the same as above. Dose-response is addressed or not, relative risk, and the confidence interval.

Q. How many cohort studies did you evaluate?

A. This represents three cohort studies, even though there are five lines there. Gonzalez was from the Sister Study, Houghton was the Women's Health Initiative study I'm very familiar with, and the following three -- Gertig, Gates, 2008, 2010 -- all come from the Nurses' Health Study. Three publications from one study.

Q. I think you mentioned the cases would be the number of ovarian cancer cases regardless of the

number of women that were enrolled?
A. That's right. Again, it is the key variable for knowing how to interpret these studies. Gertig 2000 when that study was published, there were 307 cases. The next study, Gates 2008, they chose 210 of those cases to put in another study. It is not really an update. Gates 2010 had followed the women longer, and by that time there were 797 cases.
Q. We'll discuss those a little bit more in a little bit.
While you were discussing the tables and the relevant parts of that table, there is something called the p-Value. What is the p-Value?
A. The p-Value is not presented here but some studies did show them in the data. P-Value is another statistical tool that gives us an idea of how to interpret data. So a p-Value refers to the likelihood of rejecting hypothesis that there is no association. We call that the null effect. That's exactly what the p-Value is. So the p-Value ranges between zero and 1. If a p-Value is, for example .05, that tells us that on an estimated five times out of 100, we would make a mistake by saying there is an effect when there really was no effect. That's a small amount. If a p-Value was .5, that tells us half the time we would make a

mistake by rejecting this, what we call null hypothesis.

The statisticians that developed the tool advised that people present what the p-Value is rather than using any particular cut point.

Q. "Cut point"?

A. Yes.

Q. What does that mean?

A. Some scientists over time have developed -- I'm trying to think of the word.

Q. Convention?

A. (Continuing) -- convention. Thank you. Have commonly used a p-Value at certain levels and said above that level is not statistically significant. Below that level is statistically significant.

Q. And what's that number, what's that convention?

A. There are several conventions, but one that is commonly used is P equals .05. If it's that or less some people would say that's a statistically significant result. If it is above that, they will say that is not statistically significant.

Q. What is the difference between a p-Value that is less than .06 versus a p-Value that is less than .05?

A. Virtually nothing. It just means six times out of 100 you would make a mistake by rejecting the

hypothesis that there is no effect versus five times out of 100. So, in reality, the statisticians tell us and the American Statistical Association came out clearly saying this is what you should do is say what the p-Value is and not use a line in the sand to say one is a valid result and one is not a valid result; one is reliable and one is not reliable. We don't talk about p-Values here in the relative risk for individual study. But later on, when we talk about dose-response, we will be presenting some p-Values.

Q. Would it be appropriate as a scientist to dismiss studies due to their p-Value?

A. I believe it would be especially when you are looking in the totality of evidence than to say one study is statistically significant and one is not, and, therefore, to dismiss the one where the p-Value is greater than something doesn't give you the full picture. You really need the full picture.

Q. Would it be inappropriate methodology to dismiss as a finding a result that is not statistically significant?

A. To dismiss a study that is not significant, not statistically significant? It would be inappropriate to dismiss that, yes.

Q. It would be inappropriate?

A. Inappropriate.
Q. Dr. McTiernan, looking at this forest plot of both case-control and cohort studies, what does the data from this forest plot of the epidemiological studies that you reviewed both case-control and cohort tell us about the consistency of the data from your review?
A. It tells me it is remarkably consistent because you could see that almost all of those relative risk data points are to the right of the line. They are all indicating increased risk in ovarian cancer in women who used talcum powder products compared to women who do not use them.
Q. That's regardless of study design. Is that correct?
A. Yes.
Q. Did you evaluate the role of chance as a possible explanation for these study results, and if you would tell us what does chance mean?
A. You evaluate chance by looking at totality of evidence. You can't really tell chance by any of these individual statistics. It is not the correct way to evaluate a statistic to say it only tells you about chance. The p-Value is really just how incorrect would you be to reject a null hypothesis.

Q. Now, in addition to the cases of all ovarian, did you look at any subtypes of ovarian cancer?
A. We did. There are different types of ovarian cancer. 90 percent of ovarian cancers are epithelial. That's the surrounding area, the outside area of the ovary. Of those 70 are what we call serous, and there are smaller percentages of other types of cancer. There is enough data in several studies to look separately at those women who develop serous ovarian cancer compared to those -- in this case compared to controls.
Q. From your review of the case-control and cohort study, looking at serous ovarian cancer, were you able to render an opinion regarding the consistency of those study results?
A. Yes. This slide has both the overall on top but then the serous cancers on the bottom. You really can see again remarkable consistency. The relative risks are all to the right of the line under serous. You really see it is a consistent finding.
Again, on this slide we also just indicated the relative risk and the confidence intervals. You see this across the study types. You do see wide confidence intervals for the serous, and that is because these sample sizes are much smaller than for

the overall cancers. You can see this in this graphic. If you compare the top, they tend to have more narrow confidence intervals, more precise. It is wider in the bottom because they are smaller studies. Sample size really matters. The reason why they are smaller, only about half the women in the studies that can look at this were serous.

Q. Again, to be clear, for instance, at the top when you have that tight line, is that more precision or less precision?

A. More precision.

Q. Of the smaller line?

A. Yes.

Q. Give us an example. And a broad line would suggest what?

A. A broad line tells me it is a smaller sample size and that there is less precision in that estimate. But, again, it doesn't affect the relative risk. It just affects what might happen in the totality of what the real result might be if you had the universe.

Q. Dr. McTiernan, now that we have looked at the data from the case-control and the cohort studies -- and would you call that source data?

A. Source studies.

Q. -- is there a standardized way to look at the source studies overall or in the aggregate?
A. Yes. Meta-analyses are very useful, and in this case we have seven meta-analysis that had been published by the time I prepared my expert report, and an additional study was made public after my report was published. That's the one at the top called Taher.
Q. You published meta-analysis and pooled analysis?
A. I have, yes.
Q. Tell us the importance or not of the information that you gleaned from the meta-analysis and the pooled studies, its advantages and disadvantages.
A. So we presented much of the same data on this slide for the individual studies with some differences. So, again, the study name and year is presented. We also wrote the number of studies available in the next column. This study, if you look at the first meta-analysis that was published in 1992, there were only six studies available at that time. As we go up by year, you see more studies available. By the time we get to the most recent meta-analyses, they have the largest number of studies. 27 studies in each one.
Q. As you move up from Harlow in 1992, are you

looking at the same study, the studies that were included in Harlow and some additional studies?

A. Yes. Each newer meta-analysis would subsume the other studies below. So we look at all of the studies. It is important to look at them and see what was the knowledge at the time it was published. But the most valid, in my opinion, studies to look at are going to be the three most recent. They all have 27 studies in them. They are very comprehensive.

We also included the number of cases in the next line where they were available. You can see from the top two studies we have many more cases available than were available for the individual source studies, 17,000 and 14,000 respectively.

Q. Those are actual cases of ovarian cancer?

A. Cases of ovarian cancer, yes.

Then we looked at whether they evaluated for dose-response and then what the summary relative risk. This is a relative risk calculated from the individual studies data and their confidence intervals.

Q. What does this information with regard to the relative risk of the studies -- how does this inform your opinion with regard to the totality of those meta-analysis and pooled studies?

A. This really helped form my opinion because I was

able to see what the data looked like overall, what's the overall summary of what is happening in terms of risk of ovarian cancer in talcum powder product users compared to non-users.

Q. What information does it provide you with regard to the strength of the studies?

A. It tells me the strength because of the consistency across those studies and it tells me a precise number. I like to think, What is the relative risk? In this case it ranges between, for the most comprehensive studies, this ranges between 1.22 to 1.31. That's between a 22 to a 31 percent increased risk of ovarian cancer in product users versus non-users.

Q. You got Langseth there that says 1.35?

A. Langseth was older and there are 20 studies there. So it's not the most comprehensive.

Q. You have Terry below there under pooled. Did you consider the totality of the meta-analysis and the pooled analysis?

A. I looked at both. Terry is different. We have it separate because it is a different type of study.

The pooled analysis, again, is when investigators share the actual data with the coordinating center. They have the opportunity of

having all the data on talcum powder products and on ovarian cancer, but they also have information about other variables to adjust their study for different variables in case that could affect the result.

Q. When you adjust their study for different variables what are you speaking of?

A. Sometimes in studies with humans when you are trying to determine what effect some variable might have on disease, there could be intervening variables. We call them potential confounding variables. That's the type of variable if it is associated both with the disease and with the exposure it could be influencing results.

Q. Give an example.

A. An example might be, a commonly used example is cigarette smokers and lung cancer. If you did a study and you determined that individuals who carry matches have increased risk of lung cancer, you may be misinterpreting the data. And it is really about smokers who carry matches, and it is the smoking that causes lung cancer.

That is just one example. In that case, you might want to adjust for those variables, and you find out matches don't cause lung cancer.

Q. As you reviewed the various studies, did your

part of your systematic analysis include ruling out -- rather, examining the studies to see whether or not confounding was addressed and whether it was adjusted for confounding?

A. I looked at that. In all but one of the case-control studies presented the information on confounders. The problem with confounding, you can't assume from reading the paper that these are all the potential confounding variables because the studies will present the confounding variables and they will present them for their data for their own study; and you can't assume something should be a confounder, if it wasn't in that study. It's always study specific, the confounding.

I did go through the exercise of looking at those individual studies that had reported on when they took the confounders into account and when they didn't, when they had a relative risk that was just a plain old relative risk and then had one that was adjusted for these confounders and ten presented both of those types of data, and the relative risks were almost identical in all but one, and that one only changed, that relative risk changed a small amount. That tells me if the relative risks don't change with adjusting for confounding, then it really wasn't a

problem in their study. If the relative risk looks the same after adjustment, then it didn't affect the relative risk.

Q. Thank you.

A. That was one of the benefits of a pooled analysis. You can check all that information and you can adjust fully for all of the potential confounders you know about.

The Terry study, it's a pooled analysis, and it tells us they had 8,525 cases, a large number, and it tells us they found a 24 percent increased risk of ovarian cancer in using the statistical term, it was statistically significant because the confidence interval does not include one.

Q. Dr. McTiernan, one last question, and we will keep moving in the interest of time.

Looking at the relative risk for all the meta-analysis and the pooled analysis, did any of the lower bound confidence intervals, were any below 1?

A. No.

Q. What if any information did that provide?

A. If you use the common terms, it would be the always statistically significant. The ones at the top have -- are much more narrow and that tells me sample size is bigger. There is more precision to those

estimates in the most recent ones. So I relied more heavily on those more recent meta-analyses and the pooled analysis.

Q. Before we go on and touch on the various studies, I believe you -- did you do a forest plot for the serous group?

A. Yes.

Q. Again, why did you select serous versus some other type of epithelial ovarian cancer?

A. It was the most common subtype available in these various studies, the most common data and most common presented in these studies. It accounts for about half of all ovarian cancers. It is a very relevant one to present.

Q. If you can sum up what this information tells us with regard to the study findings.

A. It suggests the relative risk of serous ranges between 1.24 -- I'm going to say 32 because while Taher influences me, it is not yet published, but it is very interesting it is also in the same range. So increased relative risk of serous cancer with talcum powder product use. The confidence intervals are narrow. It tells me it is a precise estimate.

Q. What does that information tell you about the strength of the evidence?

A. It tells me exact numbers. I like to use that to know what the exact level of increased risk is, 1.22 to 4-to-1.32.

Q. You look at the number?

A. I look at what the relative risk is telling us what the data is showing.

Q. So strength, in your opinion, is equated with the relative risk number. Is that correct?

A. Yes.

Q. You've talked about the various case-control, cohorts, meta-analysis, pooled analysis. What is replication?

A. Replication would be different, in different types of research. But in epidemiology we don't just replicate results. We look at totality of evidence. So somebody might publish a study. We wouldn't necessarily design and produce an exact replica of that. What we do is determine a question, design a study, look at important variables, and then look at results. But when you see similar findings across different studies, across different areas, that is akin to replication. It tells you that you have reliable findings.

Q. Dr. McTiernan, what I want to do now is just move briefly into a few of the studies, if I may.

First, is there a perfect study?
A. No.
Q. How many cohort studies did you say you looked at?
A. The three cohort studies.
Q. Did you examine for purposes of your opinions not only the three cohort studies, but their strengths and weaknesses?
A. I did, yes.
Q. Did you do that as well for the case-control studies?
A. I did.
Q. Briefly walk us through the cohort studies, tell us the basic background, what the strength and weaknesses are. And we're going to do the same generally about the case-control and then move on to Bradford Hill.
A. The three cohort studies were conducted in this area. The first was Nurses' Health Study. In their analysis they included 78,000 women. By the time they did their analysis, they had 307 cases of ovarian cancer developed. They collected their information on the talcum powder product use in 1982. They did not update it. Their question was on powders in general.
Q. The questionnaire?

A. The questionnaire was on powders in general including talc and other powders. It was not updated. They asked about ever use, how often they used it, but they didn't ask for how long they had used it.

Overall, for ovarian cancer they found a relative risk of 1.09. They did not see a dose-response.

And for serous, they found a relative risk of 1.4. So this was comparing users versus non-users.

Q. How do you evaluate those numbers? Are those positive numbers? Negative numbers?

A. Yes. Both in the positive direction for confidence interval for ovarian cancer including 1; confidence interval for serous did not include 1.

Q. So for serous ovarian cancer, if you use the nomenclature "statistically significant," was that study statistically significant?

A. Yes.

Q. For ovarian cancer, was that a positive or negative finding?

A. It was a positive relative risk, but not statistically significant, if you use the criteria of crossing 1.

So strengths of cohort study for this specific instance that it limits recall bias. Recall bias is a

theoretical problem for case-control studies. If cases remembered use of something of a talcum powder product differently than controls do, a prospective cohort study is unlikely to have recall bias because the women don't have ovarian cancer when they enter a study.

There were some weaknesses, and I've listed them here. They were missing quite a bit of data. They didn't ask about duration of use. Their exposures were potentially misclassified because they didn't update. If somebody was classified as a nonuser at study entry and they started using, you wouldn't know that. If they were classified as a user and stopped, you wouldn't know that.

Q. What would that do to the relative risk?

A. It would attenuate it, lower it. It would make it look like it's closer to 1 than it is in fact.

This is an issue for incomplete data for either case-control or cohort studies. In these cases where the cohort studies did not update their data, we call that that they had insufficient exposure level, and it could make the relative risk look lower.

Q. The relative risk may look lower than what it actually is?

A. Yes. Small sample size gave it insufficient

power, and power is a statistical term to describe how you need larger sample sizes to find the relative risk, and it was nurses only.

I won't talk about the middle study. It was really just a subset for doing a genetic study.

Gates 2010, they followed women until they developed ovarian cancer, by this time 797 women. All of the issues about this study are the same as the first publication with one exception. Under "findings" they chose to use a different way of classifying the participants. So instead of comparing users to non-users, they added together women who had used a little bit, who had used less than once a week to the non-users.

Q. So in Gates 2010, they combined someone who was not a user with someone who might have used the product less than one week?

A. Yes.

Q. What does that do to the relative risk?

A. That would attenuate the relative risk as well.

Q. It could drive the risk down?

A. Yes.

Q. Please.

A. So, otherwise, the other issues are the same. They found a relative risk of 1.06 for overall ovarian

cancer and for serous ovarian cancer.
Q. That relative risk of 1.06, is that a positive relative risk?
A. It is in the positive direction confidence intervals include one.
Q. The weaknesses that you just discussed with Gertig 2000 would be very similar with Gates 2010. Is that correct?
A. Yes.
Q. Let's move to the next cohort study that you reviewed.
A. This is the Women's Health Initiative, one I know very well because I was the project director and very involved with this study when the questionnaire was developed, and procedures and protocols were developed.
Q. How long were you involved in that study?
A. 15 years altogether. I was project director for five years; and after that I continued to lead the outcomes evaluation part of the study. So this study had 93,000 women when it began; and by the time the data collection was completed for this particular study, 429 cases of ovarian cancer had occurred. The women completed information on use of powders similar to the Nurses' Health Study by self-administered form

and by asking about general question about powders to the private area. The questionnaire asked about duration but not frequency.

Q. What's the follow-up to that?

A. 12 years. And, again, it was not updated. So if somebody changed their exposure, you wouldn't know it. If they became a user, you wouldn't know it. If they became a nonuser, you wouldn't know it. The impact of that is to lower the relative risk or to move it closer to 1.

Q. What were the findings?

A. For all ovarian cancer there is a 12 percent increased risk similar to serous cancer, 13 percent increased risk, but the confidence intervals included 1, positive relative risk.

Q. Weaknesses? Strengths?

A. Strength, again, limits recall bias. The weaknesses are very similar to what we see for the Nurses' Health Study. There is a power issue because of the small sample size. Here sample size is key, the number of cases that develop. In a cohort study, the only reason for enrolling so many women in a study is to get enough cases. In this case 429 cases is the important number. It was small compared to what you need.

Q. Going through those five weaknesses, missing data, what does that do to the relative risk? Does it drive it higher?
A. It would drive it lower, make it weaker, closer to 1.
Q. Exposure, not updated. What would that do to the relative risk?
A. Same thing. That would be part of incomplete exposure information, it would attenuate it down.
Q. Insufficient power number of cases?
A. Same thing. Not enough numbers. It is more difficult. If you have a smaller sample size, it is more difficult to find the relative risk in this range that we're looking at. We're looking at relative risk 1.2 to 1.4; and to find that in studies, you need a larger sample size.

THE COURT: I have a question, Dr. McTiernan, before we go on.

For instance, when you indicated incomplete dose-response analysis, you said you were the project director for this. You pointed out these are weaknesses. Why was it constructed in this way?

THE WITNESS: Excellent question. The Women's Health Initiative was designed like many cohorts to look at so many different outcomes, heart disease,

fractures, breast cancer, colorectal cancer. So we had to look at variables, risk factors for all of those.

So in an ideal form questionnaire you would have details on every single variable to a great degree, as much data as you can collect. This was a government contract, and the government limited how many pages we could ask the women to complete. It was a paper issue. And so we really -- the committees that worked on this had to limit the length of the questionnaires, and that meant limiting how much information we could collect on each question. Perineal products use is really only relevant to gynecologic cancers. It wasn't asked for purpose of looking at heart disease or breast cancer.

THE COURT: So what you're telling me, this was an initiative that was not specifically directed towards talc and ovarian cancer. There were a lot of other health issues being addressed, a much broader study?

THE WITNESS: Yes. You described it much better than I do. Thank you.

But the same is true for the Nurses' Health Study and Sister Study. They weren't designed specifically for ovarian cancer. By design,

case-control studies are designed for ovarian cancer. That's one of the strengths of a case-control study, strength of a cohort study, is that it is prospective, limits this recall bias issue.

THE COURT: For a cohort study, that was only directed to the one issue that would be different?

THE WITNESS: If you could do that, yes. There aren't too many, but some of them do.

THE COURT: Thank you for clarifying there are other studies broader based as well.

BY MS. PARFITT:

Q. Let's move on to the last cohort study that you examined.

A. Gonzalez was the cohort study called the Sister Study, and to be in the study an individual had to have a sister with breast cancer; and this is a government-run study, and the main goal is to look at risk factors for breast cancer.

So the sample size is designed for breast cancer, and many of the questions are designed for breast cancer. They asked women when they entered the study whether use of talc was in the 12 months before enrollment, and they followed the women for just six years before they decided to analyze these data.

Q. 12 months before the study, what is the

significance of that?
A. It is very low exposure data, and the resulting data are consistent with that. Only about 13 percent of women said, Yes, I used talc, because they only asked about 12 months. So if they asked about lifetime or ever, they might have gotten a larger number, but they only found out for 12 months.

So by the time they followed these women over six years, they had 154 cases. One thing that's very important about this study is that they didn't confirm many of the cases. They only confirmed about two thirds in fact had ovarian cancer. I didn't mention the other two cohorts were very good and did confirm ovarian cancer. That's really critical to know: Did this person really have ovarian cancer? So the results are no dose-response information in the study.
Q. Some people have referred to this as the "doucing" study. How did douching weigh into the results of the Sister Study?
A. They did find douching did increase risk. It was also douching in the last 12 months. But then they adjusted for that variable and other potential confounders and found it didn't affect the results. With or without adjustment for douching, the relative risk was approximately .7. It was below 1, but it

didn't change by adjusting for it or not.

Q. So based upon this study, what information does it provide you with regard to studies in general, adjusting or not adjusting for douching, and how that might impact study results?

A. It tells us for this study it was not a confounder. It didn't affect, even though it was related to the disease and related to the other exposure, it didn't make any difference to adjust for it.

In terms of strength, the same strength as the other cohort studies. One of the main issues in my mind is the very small sample size, 154 cases only, and that there was a poor confirmation of cancer diagnosis.

Q. What would those limitations do to the relative risk?

A. Again, it would attenuate relative risk.

Q. Let's move quickly, if we can, to the case-control studies, and then we'll try to get down the home stretch here.

There are some case-control studies we're not going to describe each individual one. Did you take into consideration the limitations and strengths of all of the case-control studies as well?

A. Absolutely, and I wrote about each one in my report.
Q. In the meta-analyses and the pooled?
A. Yes.
MS. PARFITT: Your Honor has your report.
Q. So if you can briefly discuss what they are and we could move on.
A. Strengths of this is the ascertainment of cases was excellent. I should mention the control of the cohort studies, two of them had excellent ascertainment of cases. Most of the case-control studies had detailed lifetime exposure information on talcum powder product use. Many were population-based, and those are generalizable to the population from which they are taken.
The larger case-control studies had what we call sufficient power to determine the relative risk that we are looking at, 1.2-to-1.4. The potential limitations, some of them did have insufficient power, some were very small, especially the older studies.
As the newer studies came along, they realized they needed to make their studies larger, and there were. There was some potential for exposure misclassification here as well, if the study didn't ask about fully, about lifetime use or if the women

didn't recall.

Case-control studies always have the potential for recall bias. Some methodologists say that's more of a theoretical reason.

Q. What does recall bias mean?

A. If the cases remember something more or more easily than do the controls, there could be a bias between their findings, between their results. Again, the methodologists that look at this say it is more theoretical but it is still something to consider.

Q. Based upon your review of all of these case-control, cohort studies, the study designs, what is your opinion with regard to whether or not recall bias impacted study findings?

A. I think it is less likely because you have such consistency across studies. What is interesting is that within studies, those that we're able to look at type of ovarian cancer, this finding was seen only in epithelial ovarian cancer, not in the other types. There is a small number of cases that were not epithelial. You didn't see that association with talcum powder product use. If a woman with ovarian cancer is more likely to recall use of these products, you would expect to see it across all types of ovarian cancer and you didn't see it in all types.

Q. And you didn't see that?
A. And you didn't see it in all types. In all epidemiologic studies there is potential for confounding, and that's when an intervening variable is affecting the results. So I considered that in all and looked to see whether they had adjusted for confounding.
Q. Dr. McTiernan, in spite of all the limitations and strengths you considered with regard to the epidemiological studies, are you confident in your opinions talcum powder products cause ovarian cancer?
A. I am, yes.
THE COURT: Let's take our break now.
THE DEPUTY CLERK: All rise.
(Recess.)

THE DEPUTY CLERK: All rise.

THE COURT: Thank you.

ANNE MC TIERNAN, resumed.

DIRECT EXAMINATION (continued)

BY MS. PARFITT:

Q. Dr. McTiernan, when we took the quick break, we were about to begin a discussion about the methodology you employed for assessing talcum powder products can cause ovarian cancer. What is the methodology you employed in order to make your causality assessment?

A. I applied a Bradford Hill causation process which involves investigating several aspects of causation. I looked at strength, temporality, coherency, specificity, dose-response, experiment, consistency, plausibility and analogy. And then I weighed the evidence and made a conclusion.

Q. These Bradford Hill guidelines, are these guidelines that are generally-accepted and recognized by scientific bodies, both nationally and internationally?

A. Yes.

Q. Are they a checklist of items?

A. No, they are not.
Q. What are they?
A. They are aspects to consider. Some may be important for an issue and some may be less important.
Q. For purposes of your opinion, did you consider all of the nine factors?
A. I did consider them all.
Q. I would like to have you walk us through the various aspects that you considered. We already talked and spent some time on the first one, strength. My question to you is, did you, for purposes of your opinion on causality, assess the strength of your association?
A. I did.
Looking at the data overall, I concluded the risk of ovarian cancer was increased by 22 to 31 percent in users of these products compared to non-users.
Q. Is there a minimum relative risk?
THE COURT: What was the percentage again?
THE WITNESS: 22 to 31 percent.
THE COURT: Thank you.
Q. Is there a minimum relative risk for a determination of causality?
A. There is not.

Q. Dr. McTiernan, are there other examples of exposure and disease where the associations are similar to the associations you saw with talcum powder products and ovarian cancer, briefly?
A. There are several. A couple that are relevant, the Women's Health Initiative Clinical Trial --
MR. WILLIAMS: Your Honor, I don't believe this is in the report. We are checking now. I don't believe it is in the report.
THE COURT: Ms. Parfitt.
MS. PARFITT: The two she picked were in the report. Do you want me to come back to that question?
MR. WILLIAMS: That would be great.
THE COURT: If there is an objection, you just stop talking until we rule on it.
THE WITNESS: Okay.
THE COURT: Thank you.
Q. You were starting to talk about HRT. Was that in your report?
MS. PARFITT: I have it in the report, page 26 and 27.
MR. WILLIAMS: Thank you, your Honor.
THE COURT: SO we're back to the same association question.
BY MS. PARFITT:

Q. A couple of examples, and the first one you started to speak about was HRT?
A. The Women's Health Initiative Clinical Trial found a relative risk of 1.26 in women assigned to a hormone therapy for five years compared to placebo. An observational study found a relative risk of 1.6 for HRT use. This is for risk of breast cancer.
Q. Any other examples?
A. Another example is exposure to secondhand smoke. I also found a relative risk in the similar range.
Q. A similar range of the 1.2 to 1.31?
A. Yes.
Q. Let's move on to the next Bradford Hill aspect. This would be consistency. Again, we talked quite a bit about the consistency earlier on in our discussion. What is your opinion with regard to whether or not the Bradford Hill consideration of consistency was met based upon your evaluation of the literature and study you did?
A. Across the studies -- and you could see it visually in the forest plot. There is a consistent increased relative risk across studies for those who were talcum powder users compared to non-users.
Q. Over what period of time?
A. Over from 1982 through 2016 and the results were

consistent across countries and across races and ethnic groups as well as consistent within the studies themselves. You also see the same consistency with serous cancer. What is clear is that the important thing to look at for consistency is the effect size, the relative risk. That determines consistency of results in epidemiologic studies.

Q. Let's move to a concept we haven't talked too much about and biological plausibility. Did you consider biological plausibility for purposes of your causation assessment?

A. I did.

Q. What is biological plausibility?

A. Biological plausibility refers to does an association make sense? Is there some plausible pathway through which exposure to these products can cause cancer?

Q. Is biological plausibility the same as biological proof and biological certainty?

A. No, it is not.

Q. Why not?

A. Biological plausibility the guideline is just that if you determine a way in which this could happen, that is sufficient to determine that a cause could happen.

Q. Based on the biology or science?
A. This recognizes biology is a moving field. At one point we may understand more biology than what we do at other points.
Q. Dr. McTiernan, do you have an opinion whether it is biologically plausible for talcum powder products to cause ovarian cancer?
A. Yes, I do.
Q. What are those opinions?
A. I believe talcum powder products, first of all, contains known carcinogens, and there is a list of them here, and IARC has been very clear that asbestos causes ovarian cancer. These several components or constituents of talcum powder products are known carcinogens, are classified as such by IARC, and these constituents have been shown through various laboratory studies and laboratory testing to be in these products.
THE COURT: Dr. McTiernan, you started by saying, talking about known carcinogens, and you mentioned the asbestos specifically. Would your opinion change if there was not asbestos in the talc?
THE WITNESS: It wouldn't change because the epidemiologic studies only asked about talcum powder products. They weren't able to ask the women, did you

use asbestos? That is all from the product itself, talcum powder product.

BY MS. PARFITT:

Q. Dr. McTiernan, did you review any documents in preparation for the opinions with regard to the components of talcum powder products, just briefly?

A. I did. I reviewed some published literature. I reviewed some testing documents that were provided to me by you and your colleagues showing that internal testing by J&J and testing by Dr. Longo.

MR. WILLIAMS: Objection to this line of questioning concerning the J&J documents for purpose of this hearing.

MS. PARFITT: It was foundational, how she finished forming her opinions --

THE COURT: I'll let her talk about what she reviewed without getting into the documents.

BY MS. PARFITT:

Q. Did you review internal J&J testing documents?

A. Yes.

Q. Did you also review testing documents by Dr. Longo?

A. Yes.

Q. Did you also review testing documents published in the peer-reviewed literature?

A. Yes.
Q. And you reviewed IARC?
A. I did.
Q. Having reviewed that information, did you satisfy yourself that talcum powder products that Johnson & Johnson manufactured may contain these component parts, these carcinogens?
A. Yes.
Q. For purposes of your opinion in this case, have you made -- do you have the understanding that the talcum powder products includes whatever is in the talcum powder products, whether that be asbestos, heavy metal and fragrance?
A. Yes.
Q. What is your next opinion?
A. First, that the exposure that talcum powder products can reach the Fallopian tubes and ovaries, it is an open system and there is evidence that genital application can migrate up through the genital tract. We know from -- and in addition, these substances can be inhaled and spread through the lymphatic system and circulatory system.
Q. What are the two pathways?
A. Genital application and inhalation. There has been scientific clinical studies showing in humans --

we'll talk about migration -- that several clinical studies in humans show that application of particles of similar size to talc when applied to the genital tract can move up to the Fallopian tubes and ovaries. I keep saying "Fallopian tubes," which is relevant because some ovarian cancers start in the Fallopian tubes and then move up to the ovaries, so both Fallopian tubes and ovaries are relevant.

So the substances have been applied either -- the substances themselves or a radioactive substance or powder on gloves, and these were all when women were about to have surgery, these substances were applied; and when the women had surgery, hours or days later the substances had migrated up.

Q. Does that include talc particles as well?

A. We know that talc is present in ovaries. It was shown to be present in several ovaries, and it was shown to be present in lymph nodes, in the area around the ovaries. We know that in one study found that after correcting for the surface contamination, possibly in lymph nodes in that area, that inside the lymph node there was talc, and it was highly correlated with whether the woman reported use of talc, that was McDonnell 2006 I listed there.

Q. That's pathology?

A. Pathology and clinical because the women reported their use or not. Yes, so talc is present there. It is in there. The studies have shown that substances can migrate.

The reasons the studies were not able to apply talc and see if that migrates, it wouldn't be ethical to do that. They chose other substances, and many of those were fertility type of studies. They were able to do those tests and see what happens.

The regulatory bodies also state that migration is a plausible method for the substance talcum powder product to reach the ovaries and Fallopian tube, and the FDA stated it is incontrovertible that it can migrate.

The next step I considered is what is a possible pathway for carcinogenesis, and one I'm interested in that I think is plausible is inflammation. We know from clinical studies that talc when injected into the human body causes inflammation. So there is a medical use of talc called. It's called a pleurodesis study. This is for two types of patients that develop air around their lung. It's called pneumothorax. Some of those patients have spontaneous pneumothorax and some have it because they have a serious disease. When talc is injected into

that area it causes inflammation that causes adhesions, and that's why it is used as a one-time treatment. That inflammation shows up in the blood within hours. So we know that talc causes inflammation. Numerous animal studies show inflammation and carcinogenic processes consistent with carcinogenesis.

We know cell culture studies have shown that talc applied can cause changes to cells that change the genetics. We call it epigenetics. That can make those changes that are premalignant and then can lead to carcinogenesis.

Q. You said epigenetics.

A. Epigenetics. Cancers of genetic disease, but only about 10 percent of cancers are caused by genes you inherit from your parents.

Other genetic causes are environment, and talcum powder products is one environmental cause that can affect the cell's genome and cause cancer that way.

Q. Any other credible scientific evidence that you reviewed generally to support your opinion talc causes an inflammatory pro-carcinogenic biologic effect in the body?

A. Yes. We know from the in vitro and animal

studies that that can happen, and we know women who have high inflammation in the blood have increased risk for ovarian cancer. Many of these cohort studies have shown that. We know women with inflammatory conditions -- endometriosis, pelvic inflammatory disease have increased risk.

Q. Dr. McTiernan, have you included on your demonstrative some of the studies that support both pathologic studies, clinical studies, animal studies, and in vitro studies to support this cascade of events?

A. Yes.

Q. At the end of that, what happens?

A. At the end of that, after inflammatory response --

Q. What is the role of inflammation on oxidative stress, those things you have spoken about in the pathogenesis of cancer?

A. Inflammation, the process of that can cause oxidative stress that then can cause genetic damage and then cause cancer.

MS. PARFITT: Dr. McTiernan -- and for the Court, I made a misstatement on my McDonald. I have 2006. That should be McDonald 2019.

(Pause.)

MR. WILLIAMS: Our objection, your Honor, is that the McDonnell study was one that was discussed expressly with the Court in chambers on a couple of occasions. It was listed on two other witnesses' supplemental lists but not on Dr. McTiernan's list. It was not referenced in her original report either. Our objection is, for purposes of Dr. McTiernan's testimony, it is not appropriate based on the Court's previous ruling for her to testify concerning it.

THE COURT: Was it on her supplemental list?

MS. PARFITT: Yes. It says "all briefing."

THE COURT: No, no, no. Did she list that particular study on a supplemental list?

MS. PARFITT: No, we did not. We listed it with the briefing. It came out after her report, after her testimony.

THE COURT: I think you had some very specific things listed and it is not there.

MS. PARFITT: Because it was in the briefing we didn't do that. So we could move on.

THE COURT: Let's move on. Even though you did it in the context of correcting the data on the McDonald study, but we will not be discussing the McDonald study as something you relied on.

BY MS. PARFITT:

Q. Dr. McTiernan, do your opinions change with regard to whether or not it is biologically plausible for talcum powder products to cause ovarian cancer if you did not consider the McDonald study?
A. My opinions don't change at all, and my expert report was completed before that paper was published.
Q. Thank you.
Let's move on to the next.
THE COURT: Did you complete your questioning? I want to make sure where you were. You got interrupted about the date of the report. I want to make sure.
Q. What role does inflammation and oxidative stress have in the pathogenesis of ovarian cancer?
A. Oxidative stress, it starts a cascade of DNA damage, and it is one explanation through which inflammation can cause ovarian cancer.
Q. Dr. McTiernan, in the course of your review and study and opinions, did you also consider studies that perhaps disagreed with your opinion with regard to whether or not talcum powder products can cause ovarian cancer?
A. Yes.
Q. Did you take that into consideration in rendering your opinions?

A. Yes.
Q. Moving on to the next aspect of Bradford Hill, and that would be dose-response, otherwise known as biological gradient. What is dose-response?
A. Dose-response is the question of whether the increase in use of some product or increasing exposure is associated with a change in level of relative risk. In this case, our question was: Does increasing use of talcum powder products increase risk of ovarian cancer?

One study that was able to look at this, because they had such large numbers, was the Terry study. We'll use that as an example of dose-response.

One way to do dose-response is among people who are using the product, to divide them into categories, and then look across those categories, compared to never users, what is the relative risk of ovarian cancer in each of those categories.
Q. Before you do that, what's the optimal metric if there is one for dose-response?
A. Relative risk in epidemiological studies, we look at relative risk. And so in the Terry study, they divided women into four categories by level of use of talcum powder products, and compared to never users. On this table, the letters "OR" stands for

odds ratio, and that's the same thing as relative risk.

So what they are able to see, those women who had never used. The number there is 1. That means they are the comparison group. When you see -- when you look across the quartiles, that's --

Q. Do you have a pointer?

A. -- increasing level of use, and he's outlined it nicely, you see the relative risk for the first category is 1.14; for the second, 1.23; the third, 1.22; and the fourth, 1.32. This is risk of any ovarian cancer by level of use.

You see that the level goes up. 1.14 is higher than 1.1, 1.23 to 2, are higher than the first category, and the highest is the top category.

The authors' calculated confidence intervals for each of those levels of relative risk, and they all show significance or near significance meaning they don't include 1. The first category does, and that's why it is often called "near significant." That's how some people would describe that.

And then there is another statistical tool that is often used in dose-response to calculate how likely this trend would be -- sorry. It tells us how correct we are by rejecting a hypothesis, that there

is no dose-response. So these would be p-Values. They calculated p-Values in two different ways. This is called the p-Trend, and they included one of them here in the table, but they put one in the text.

Q. What is the significance of that?

A. What this one is, p-Trend, this is looking only at the people who used talcum powder products, just comparing those four categories, and that trend is .17. What that means is that they are estimating that 17 times out of 100 you would make an error by assuming there was a dose-response when there really isn't.

I'm about to talk about the other p-Trend which they describe in the text. If you compare those categories to the non-users, the p-Value is less than .01. That means it would be less than 1 time out of 100 that you would make a mistake by saying that there was a trend when there really wasn't.

So three different ways of using a statistical tool to help you interpret them. I interpret this as showing dose-response. It shows the relative risk confidence intervals that were narrow -- that weren't terribly wide and did not include one. The statistical test compared to non-users was highly significant although the statistical test comparing

only users was not.

Q. Dr. McTiernan, would it be inappropriate methodology to include never users in that assessment?

A. I believe it is appropriate to include the never users. First of all, the statisticians advise that we do include non-users. But it would be comparable to, in a clinical trial, if you wanted to look at what effect different doses of a medicine would have you'd randomly assign people to different doses and to a placebo, and then you compare those different doses to placebo. That's kind of what we do in epidemiology, comparing it to a placebo, to people without the exposure.

So I believe it is correct to compare to that and in my studies I usually do. But I think it is very correct as they did to show all of this so that different investigators can see the data fully. So I think it's appropriate they presented two different p-Values and that they showed confidence intervals.

Q. Dr. McTiernan, is there a threshold response the public would expect?

A. A threshold of what, relative risk?

Q. A threshold of relative risk.

A. No, there is no particular one, and there are different shapes a dose-response can have. Some can

be a straight arrow -- I'm sorry. Straight up, one dose increases a certain amount. It could be like this one is, where it just shows that you see an increase at the first level, and the second and third look very similar, and the top level looks the highest. Some exposures have a curve, a U-shaped curve. So there are different types of things an exposure can do in terms of dose-response.

In this one I interpret, because the highest relative risk was in the highest dose, and you see some step-wise increase, to me it really looks like there is a dose-response.

Q. Dr. McTiernan, do you have an opinion whether a single dose of talcum powder can cause ovarian cancer?

A. I think we don't know what a dose could cause. If one piece of one application of talc got into the ovaries or Fallopian tubes and sat in there and caused an inflammation and continued because talc is unlikely to be able to be rinsed away from the body, if it continues in there and continues to cause inflammation, perhaps. But with more applications, you have an idea there is more chance of the substance being incorporated into the body, and therefore could set up inflammation and other methods of causing cancer.

Q. Is there any other example? Were there any other studies that categorized the dose-response?
A. Yes, two other meta-analyses. The large meta-analysis were able to do that, and this is data from individual studies.

So this one is from one of the recent meta-analysis Penninkilampi, and they were able to find most studies that had some information either on duration of use or total lifetime applications. When they looked at the 12 studies who had duration of use, they looked at for those women who used for more than 10 years compared to less use, the relative risk was 1.25. So that tells us long-term use has an effect. Five of those studies they included the meta-analysis had total lifetime applications. So it's frequency times duration. And they divided those into two categories corresponding to daily use for 10 years. So 3600 total applications more or less, and you did see an increase. You see a relative risk of 1.32 for the lower group users and 1.42 for the higher, and this is compared to non-users. The confidence intervals did not include one, so they are statistically significant.
Q. Is there another way of categorizing dose-response other than classifying these core files

and frequency duration?

A. Another thing researchers often do is modeling, and they will take all the information and do some statistical models to smooth out curves and get an estimate of where the risk increases with increasing, in this case, either duration or frequency. So the Berge study meta-analysis looks at the studies that had duration, and what they are modeling, they were able to estimate that the relative risk was 1.16 for each 10 years of use, also statistically significant. And for the studies that had frequency for each one dose per week, used one time per week, a relative risk of 1.05, a 5 percent increase, also statistically significant.

So this tells me there is a dose-response effect looking across these different ways of doing it, and that it is consistent across studies -- sorry. I was about to say something else, but I forgot.

Q. Dr. McTiernan, you talked about these studies that demonstrated an increased dose-response with increasing use and duration. Does Bradford Hill require there be a finding of dose-response?

A. No, it does not.

Q. And based upon the totality of your review of the studies, let me ask you this: Did you look at

studies that did not look at dose-response?
A. I did. Some studies didn't look at dose-response. Some looked at only frequency or duration, not both. Some looked at dose-response and found no effect, and some looked at it and found effect.
Q. Based upon the totality of your review of those studies that looked at dose-response, didn't look at dose-response, or looked at dose-response and couldn't find it, what is your opinion?
A. Looking over all, there is a dose-response particularly because the meta-analysis and the pooled analysis saw that clearly.
Q. What I'm going to do, to shorten this, is put up a slide that you helped me prepare. It is the Bradford Hill guidelines. We talked about strength consistency, dose-response, and biological plausibility. What I would like you to do is briefly go through the remaining, and then, in the interest of time, tell us why you've got a weight category over there.
MR. WILLIAMS: Your Honor, we are mindful of the time. I don't see counsel cutting anything actually.
THE COURT: I think we are in major summary

stage right now.

BY MS. PARFITT:

Q. Let me ask you this: Did you consider the remaining Bradford Hill considerations?

A. I did.

Q. What was the process you went after evaluating the Bradford Hill guidelines?

A. After review, I determined that I gave high or significant weight to strength, consistency, dose-response, plausibility, and temporality. I gave moderate weight to specificity and slight weight to experiment; and for both coherency and analogy in my opinion, I weighed it less than strength and consistency.

Q. Did the evidence you reviewed satisfy the coherence category?

A. Yes.

Q. Did the evidence you reviewed satisfy temporality aspect?

A. Yes.

Q. Did the evidence you reviewed satisfy the specificity?

A. Yes.

Q. Did the evidence you reviewed satisfy the analogy?

A. Yes.
Q. And you talked about the experiment.
Dr. McTiernan, in addition to the opinions that you've shared with us today, are the opinions you shared your opinions?
A. Yes.
Q. Did you consider opinions and recommendations of other scientific and regulatory bodies who also opined on the issue of whether or not talcum powder causes ovarian cancer?
A. Yes.
Q. Did you learn anything from them?
A. I was very interested to learn that some other regulatory bodies found similar findings that I did, such as Health Canada.
Q. Were there regulatory bodies that have not opined in the same way as you?
A. There were some, yes, but they did not do a full systematic review and a full causal analysis.
MR. WILLIAMS: Objection. Foundation, your Honor.
THE COURT: Sustained.
BY MS. PARFITT:
Q. Dr. McTiernan, did you review other opinions of scientific and medical and regulatory agencies on the

issue of talcum powder products?
A. I did, yes.
Q. Other than just Health Canada?
A. I did, yes.
Q. Which ones did you look at generally?
A. IARC has looked at this in more detail, and they have done a systematic review, but it was in 2006.

I've noted IARC plans to relook at talcum powder product use and risk of ovarian cancer. They placed it in high priority. At the time they reviewed it, they only had data up until 2006, but they did a full review. So they classified talcum powders as Class II B carcinogen.

Q. Have you addressed in your report and in your testimony by deposition some of the other regulatory and scientific bodies that have also examined this issue?
A. I've looked into some of them, yes.
Q. And you have taken that into consideration in rendering your opinions?
A. Yes.
Q. Dr. McTiernan, summarize for us, interval, what your opinions are today.
A. My opinions are published studies --

MR. WILLIAMS: I object. These have already

been covered.

THE COURT: Yes. I looked back -- I think it's your last slide, and every one of these has been in her testimony. If you think there is one that is not, you could ask her specifically.

MS. PARFITT: I think you are correct, your Honor.

THE COURT: I think they have all been covered. She's already indicated she helped create these slides. I understand she's adopting what I'm seeing up there -- am I correct -- as your opinions?

THE WITNESS: Yes.

MS. PARFITT: Your Honor, at this time I would conclude my examination. And I appreciate your courtesy with regard to the time.

THE COURT: We'll break for lunch. It is 12:15. 1 o'clock.

THE DEPUTY CLERK: All rise.

(The luncheon recess is taken.)

(Continued on the next page.)

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A F T E R N O O N S E S S I O N

THE DEPUTY CLERK: All rise.

THE COURT: Thank you.

Anne McTiernan resumed.

CROSS-EXAMINATION

BY MR. WILLIAMS:

Q. Good afternoon, Dr. McTiernan.

A. Good afternoon.

Q. We have met before, have we not?

A. Yes.

Q. Let me ask you again to try to keep your voice up.

A. Okay.

Q. Dr. McTiernan, you were retained in this litigation to review the current state of scientific literature regarding talcum powder products and opine on whether those products cause ovarian cancer. True?

A. True.

Q. The reference to talcum powder products in your litigation report refers to commercially available talcum powder products and all constituent elements

contained therein. Correct?
A. Yes.
Q. Asbestos is an example of a constituent element that in your opinion may be contained within talcum powder products. Correct?
A. Yes.
Q. You are not an expert in asbestos, though. Right?
A. Asbestos, in which way?
Q. In the determination of whether a product -- yes, a product contains asbestos in the first instance?
A. In terms of testing?
Q. That's right.
A. Correct.
Q. You are not an expert?
A. Correct.
Q. For that issue you are relying on others. Correct?
A. Yes.
Q. You did not do a full systematic search for causal analysis for asbestos?
A. Correct. I was not asked to do that.
Q. To be clear, though, your opinion is that talcum powder products can cause ovarian cancer even if those

products do not contain asbestos or any other constituent element besides talc. True?
A. True.
Q. You were first approached about any involvement in talcum powder litigation in 2016. Right?
A. I would have to refresh my memory for the exact dates. I don't have them right with me. I can get them, but I don't have them.
Q. Let me see if I can refresh your memory, and I should have begun by saying there are two binders in front of you, binder 1 and binder 2, and there should also be a red binder as well. Do you have that one?
A. Yes.
Q. That red binder should have your previous testimony.
(Pause.)
Do you have the red binder in front of you, Dr. McTiernan?
A. Yes.
Q. I'll direct your attention to page 12.
MR. WILLIAMS: Permission to read, your Honor, lines 12 through 15.
THE COURT: Yes.
Q. (Reading.)
"QUESTION: Dr. McTiernan, when were you first

approached about any involvement in talcum powder litigation?

"ANSWER: It should have been 2016."

Does that refresh your memory, it was in fact 2016 when you were first approached?

A. I remember saying that, yes.

Q. And you would not have said that were it not true. Correct?

A. Correct. But even at that time I didn't have the exact dates. I didn't have documentation. It was from my memory then and it is now.

Q. You have not personally conducted any research on talcum powder use and risk for ovarian cancer as of the time you were retained by plaintiffs' counsel. Correct?

A. I had read some papers prior to that. I read two cohort studies and pooled analysis, and because my university is where some of the early case-control studies occurred, I was aware of those, but I did not do a systematic review until after I was retained.

Q. I would like you to focus on my question.

You had not personally conducted any research on talcum powder use and risk for ovarian cancer as of the time you were retained. Correct?

A. I think I was understanding the word "research"

to mean read into it. If you mean research conducting the studies, no, I did not.

Q. At the end of your testimony on direct examination, counsel took you through this chart; and at the end of the chart or on the right-hand side, there was a discussion about biological plausibility and, in particular, inflammation carcinogenesis. Right?

A. Yes.

Q. And you listed here with the assistance of counsel the basis for your opinion regarding biological plausibility. Correct?

A. Yes.

Q. The first thing you listed was clinical studies and pleurodesis studies. Right?

A. Yes.

Q. Have you looked into the studies that relate to whether or not there is a relationship between pleurodesis -- that is, the intentional injection of talcum powder into the chest cavity for lungs and the impact on cells?

A. I think in my -- I think in my documents in my report I cited to research in this area showing that pleurodesis causes an inflammatory response.

Q. Other than causing an inflammatory response, any

discussion that you are aware of or studies you are aware of as to the impact on human cells of talc being applied to them?

A. I think I want to look at my report and see what I said about pleurodesis.

Q. Take a look in your book. In the first notebook it is Exhibit McTiernan 5-09, actually, the second volume, Volume 2, and it is McTiernan 509.

(Pause.)

Have you ever seen this study before, Doctor?

A. I don't believe I have.

Q. This study you will see it is called the Nasreen study. It is from the year 2000, and I'll direct your attention to the very beginning of the tab it says:

"Pleurodesis with talc is an accepted method for the treatment of systematic pleural effusions secondary to mesotheliomas."

Do you see that?

A. Yes.

Q. I want to direct your attention a few lines down it says:

"The present study was designed to evaluate if talc directly affects cell death of malignant mesothelioma cells or normal pleural mesothelial cells PMC."

You are familiar with the process of pleurodesis?
A. Yes.
Q. Let's go to the bottom, the part we highlighted down below. It says:
"Talc did not induce apoptosis."
You understand, by the way, apoptosis is planned cell death?
A. Yes.
Q. (Reading.)
"Talc did not induce apoptosis in PMC," and those are the mesothelial cells.
A. Pleural mesothelioma cells, that's what it states.
Q. That's what it referred to the PMC?
A. Yes.
Q. (Reading.)
"And glass beads did not cause significant apoptosis in either MNC or PMC."
"The present study has demonstrated that talc induces apoptosis in MMC without affecting normal mesothelial cells of the pleura."
Did I read that right?
A. Yes.
Q. Let me ask you to turn to page 5 of Exhibit 509,

the conclusion, and direct your attention to the left column at the very bottom.

Do you have that in front of you?

The Nasreen authors concluded:

"In conclusion, the significance of this study is that talc induces apoptosis in MMC without affecting normal pleural mesothelial cells. These findings also demonstrate that talc, a palliative active agent, may have a therapeutic potential in decreasing tumor burden. Therefore, it may be construed that talc not only induces pleurodesis, but also decreases the size and mass of tumors in patients with mesothelials."

Did I read that right?

A. Yes.

Q. Can you point the Court to any study that suggests with respect to ovarian cells that talc induces cellular proliferation -- strike that.

Can you point the Court to any study that was part of your analysis that suggests when talc when applied to ovarian causes harm to those cells leading to malignancy?

A. I think in my report I referred to Buz'Zard which showed that talc applied to human ovarian stromal and epithelial calls resulted in increased

reactive oxygen species, cell proliferation, the excessive growth of cells, and neoplastic transformation of cells. So ovarian cells, not pleural cells.

Q. Any other study besides Buz'Zard for that purpose cited in your report?

A. That's what I have here, yes.

Q. Let's take a look at it. It is Exhibit A 16 and in your book it should be Volume 1.

MR. WILLIAMS: Your Honor, in your book it should be Volume 1 as well.

Q. Let me start with, first, principles.

The presence of oxidative stress in tissue does not indicate that cancer will develop. True?

A. Oxidative stress is a risk factor for cancer.

Q. The presence of oxidative stress in tissue does not indicate that cancer will develop in that tissue. True or not true?

A. My opinion is that oxidative stress increases risk for cancer. So it is something we've looked at as potentially part of carcinogenesis.

Q. Any oxidative stress?

A. There are many aspects to oxidative stress and many parts of the cascade. My understanding is that increased oxidative stress is a risk factor for

carcinogenesis.

Q. Do you remember the Buz'Zard study was to assess the effects of a supplement made from modified French maritime pine bark?

A. Yes.

Q. Have you advised anyone to start using the product related to this study which is entitled Pycnogenol? See if that is referenced in the title of the article.

Have you advised anyone to start using pycnogenol for ovarian cancer?

A. No.

Q. The ovarian cells used in the French pine bark study were genetically altered?

A. Could you point to where that says that?

Q. Let me ask you to assume the Buz'Zard study used genetically altered ovarian cells that did not have a p53 protein. Can you make that assumption with me?

A. I don't like making assumptions when we are talking about scientific papers. If you can show me where it says they were not genetically altered, that would help.

Q. In court we are permitted to ask hypothetical questions, so I would like to ask you one based on your scientific knowledge separate and apart from the

study itself.

Would you assume with the Buz'Zard study used genetically altered ovarian cells that did not have a p53 protein? Are you with me?

A. I'm with you. As a scientist, I don't make assumptions like that. I'm finding it difficult. You are trying to ask me a scientific question.

Q. I am.

A. I'm having trouble making assumptions for something where I don't know what kind of cells they used in the study.

Q. You cited the Buz'Zard study for the proposition that it showed reactive oxygen species increased if talc was applied to cells. Correct?

A. Yes.

Q. Let me direct your attention -- strike that.

The Buz'Zard study showed that the reactive oxygen species actually decreased from baseline the more talc was applied. Do you remember that?

A. I believe that was a temporary decrease, and then it increased. I would like to look at the relevant graph.

Q. It is on page 5 of Exhibit A 16. I will direct your attention to the top graph there. This chart reflects the author's findings on "Generation of

Reactive Oxygen Species From Ovarian Epithelial in Response to Their Exposure to Talc." Correct?

A. This is the study where if you look under the graph, the authors are explaining it more, that there was an initial dose dependent decrease, but as time increased the ROS generation rebounded and increased compared with values at 24 hours.

Q. Let's take a look at the graph.

You see 100 is the baseline, right, and the unit of measurement is the percentage of ROS generation. Right?

Do you see that on the Y axis?

A. Can you explain where you are seeing 100 is the baseline?

Q. Are you saying there was something else that was the baseline?

A. Just to explain what the graph is meaning.

Q. I'll represent to you there has been testimony concerning this graph, and I'll just ask you this:

Do you see as more talc is applied, and we move to the right along the X axis, that the bar charts go below the 100 line except for this one which was at 50 micrograms per milliliter. Can we agree on that?

A. Yes, I see that. I'm wondering why the authors

wrote that was a temporary decrease and this increased.

Q. Perhaps could it have been because as each of these bars for any one segment was 424, 72 and 120 hours, and in any given time period it did increase. Do you see from 24 to 72 to 120 hours? Could it be that is what they were referring to?

A. I'm not sure. I'm just reading the writing it increased over time.

Q. What we do know is all of these except for one is below the baseline. You can agree on that?

A. It looks like a temporary change from what they wrote.

Q. Are you speculating?

A. They said it was an initial dose-dependent decrease, and then that increased. That's why I'm confused. It looks like the graph and the description are showing -- the description is showing additional information.

Q. That's fine. We'll move on.

The next studies you talked about were the animal studies, and you list three. Correct?

A. Yes.

Q. And you list these as studies that supposedly support the notion that there is biological

plausibility that flows from talcum powder product use to exposure to migration, to inflammation and carcinogenesis. That's why you cited them?

A. I cited them as looking at the pieces of the carcinogenic pathway. This is one issue we see with looking at this biological plausibility. We have different pieces of information along the chain of possible biological mechanisms.

Q. I assume you cited these not because they are the worst studies you could cite, but they were the strongest studies supporting your position for your conclusion as a scientist?

A. I didn't do a systematic review on biological plausibility on animal studies. What I did was I looked for animal studies that possibly could explain the association, and I did that with either PubMed search or looking at references that were referenced in epidemiological studies and the clinical studies.

Q. You did read the studies, right?

Let's take a look at Keskin. It is Exhibit A 85.

A. Yes.

Q. Exhibit A 85 is the 2009 study by Keskin that you were just referencing. Right?

A. Yes.

Q. It's entitled, "Does long-term talc exposure have a carcinogenic effect on the female genital system of rats."

Did I read that right?

A. Yes.

Q. Do you remember in this study the researchers applied talc to rats intra-vaginally or perineally for three months on a daily basis?

A. I see that.

Q. Let's go to the findings.

Page 2, second column, second paragraph, first sentence. Finding:

"In both the groups exposed to talc, Groups III and IV, evidence of foreign body reaction and infection along with an increase in inflammatory cells were found in all the genital tissues. General infection was observed in 12 rats in the study group and two rats in the control group. Neoplastic change was not found."

This study found that there was no neoplastic change in the rats who had the talc directly placed into their ovaries. Correct?

A. Yes.

Q. The next study that you referred to on your chart is the Hamilton study from 1984. Did you read

that study?
A. Can we go back to the former study Keskin?
Q. Counsel will take you back if she wishes.
The Hamilton study is Exhibit A 53, which should be in your first volume, Dr. McTiernan. In this study the authors surgically injected talcum powder into the ovarian bursal sac of rats. Right?
A. Yes.
Q. It was not the case that talc was applied to the outside or the exterior of the rats' genital area. Correct? The talc was injected into the ovaries themselves. You remember that. Right?
A. Yes.
Q. The researchers injected the talc into 10 rats. Right?
A. This is what the abstract says, yes.
Q. And out of the 10 rats injected with talc, four of them -- less than half -- showed some kind of papillary change in the ovarian surface epithelium. Is that right, Doctor?
A. Yes.
Q. The authors concluded, though, that the epithelium covering the papillary areas was regular with no evidence of cytoplasmic or nuclear atypia. Correct? That's on page 4 of the exhibit, right

column, in the carry over paragraph midway down. That was the conclusion of the study?

A. Four of them developed papillary areas and "papillary" means abnormal growth.

Q. But any chronic inflammation that the Hamilton study authors observed in the rats did not lead to neoplastic changes?

A. They are talking about papillary areas, again, which is abnormal growth.

Q. We were just reading the portion that said it did not lead to neoplastic changes --

A. Could we see the abstract again.

Q. It is the next one.

A. Back to the abstract. I'm trying to read the abstract. This says something about this there.

Q. Sure.

(Pause.)

A. I don't see here in the abstract they are concluding they are not related. I see papillary changes. From my knowledge, "papillary" is an abnormal growth, and papillary growth could be the beginning of a carcinogenic process.

Q. Are you speculating?

A. I'm talking about my knowledge, and they talk of four of 10 animals developing papillary changes.

Q. Let's move on. The next study you cited in support of biological plausibility opinion in the case was the NTP study from 1993. Do you remember that?
A. Yes, I do.
Q. Now, you mentioned earlier today that there was an agency that had found that talc could migrate from the perineum to the ovaries. Do you remember testifying to that earlier today?
Do you remember testifying to that today?
A. Yes, I stated the FDA said migration was incontrovertible.
Q. You based that on a letter you read at one point?
A. Yes.
Q. Let's put that in front of you. That's Exhibit A 89.
MR. WILLIAMS: Your Honor, for the record, it is a letter dated April 1, 2014.
Q. Is that the letter?
A. I see it, yes.
Q. Now, in this letter do you remember there was a specific discussion of the NTP report?
A. Maybe we could scroll to it or point to it in the book.
Q. It is on page 4 of the letter under toxicology

findings. Do you see that heading?
A. Yes.
Q. There is a reference here that speaks of the NTP report concluding that cosmetic grade talc caused tumors in animals even though no asbestos-like fibers were found. The report made the following observation:
"There was some evidence of carcinogenetic activity in non-asbestiform talc from inhalation studies in male rats based on an increased incidence of benign or malignant pheochromocytomas of the adrenal gland. There was clear evidence of carcinogenic activity of talc in female rats based on increased incidences of alveolar/bronchiolar adenomas and carcinomas of the lung and benign or malignant pheochromocytomas of the adrenal gland. There was no evidence of carcinogenic activity of talc in male or female mice exposed to 6 or 18 micrograms per cubic meter. However, this study lacks convincing scientific support because of serious flaws in its design and conduct including the investigators used micronized talc instead of consumer grade talc resulting in the experimental protocol not being reflective of human exposure conditions in terms of particle size."

Do you remember reading that in the FDA letter regarding the NTP study upon which you rely?

A. I see it now.

Q. Let's go to the next page.

Do you remember the FDA letter upon which you relied said:

"Investigators conceded that they had problems with the aerosol generation system; whereby, the target aerosol concentrations were either excessive or not maintained during 26 of the 113 or 122 weeks of the study. The study did not include positive and negative dust controls which would have permitted an exact assessment of the talc's carcinogenicity relative to the two control dusts?"

Do you remember reading that?

A. I see it here.

Q. They said further:

"In light of these shortcomings, a panel of experts at the 1994 ISRTP/FDA workshop declared the 1993 NTP study has no relevance to human risk."

Did you cite that on direct examination?

A. Did I cite this statement or that workshop? I'm not sure what the question is here.

Q. Did you cite anything to the Court in your direct examination testimony to the effect that the

shortcomings of the NTP rat study would be made available to the Court?

A. I'm a little confused. I cited the study where the NTP study showed that adrenal cancers developed in female mice as well as alveolar bronchial which are lung cancers.

Q. Do you see this letter you have in front of you, the exhibit which has the FDA letter? Did you see that at the time that you formed your opinions in this case relying upon the NTP rat study?

A. I did see this, and I saw this is a letter describing officials' opinion. I didn't see the full report. I don't know what that workshop was. I don't know if they published in a peer review.

All I know, I was able to see the NTP rat study, evaluated it, saw that there was cancer developing in animals exposed to talc, and that's why I cited that. But I believe this letter also then does mention that migration is incontrovertible.

Q. Next you cited under "in vitro studies" the Fletcher and Saed study from 2018. Right?

A. I see that's here, yes.

Q. You know Dr. Saed already testified here in court, right?

A. Yes.

Q. Do you agree -- have you read Dr. Saed's testimony from this proceeding?
A. No, I have not.
Q. Let me put this in front of you and ask you a question. This is the transcript from the other day from the examination of Dr. Saed. You see there it is on page 119 of the transcript from the other day.
A. Is this a final transcript?
Q. It is. My question to you is: Do you agree with Dr. Saed that prior to his analysis in 2018 and the work that he has done in connection with his retention by the plaintiffs' counsel in this matter that there was not enough evidence to establish a direct link and precise mechanism developing in association between talc use and ovarian cancer?
MS. PARFITT: Objection, your Honor. I do not believe we have a final sworn copy of that transcript. She's been asked about testimony out of context. One section of Dr. Saed's has nothing before or after that, no foundation what Dr. Saed had said.
MR. WILLIAMS: I'll ask the question separate and apart from the transcript.
THE COURT: I don't know if you reserved the righ to review the transcripts. I believe these are final transcripts.

(Pause.)

THE COURT: So they have to go over them.

MS. PARFITT: The other would be, I don't believe Dr. Saed looked at the NTP study. It goes to my response; it is one question taken out of context with all of Dr. Saed's testimony having no idea whether Dr. Saed looked at the NTP study.

THE COURT: I think he moved on from the NTP. I think he went on to another study, the Fletcher/Saed study.

MR. WILLIAMS: That's correct.

BY MR. WILLIAMS:

Q. My question to you, separate and apart from what the final transcript will reflect, is Dr. Saed's testimony: As you sit here today, as a scientist, do you believe that as of 2018, there was not enough evidence to establish a biological mechanism, or, in particular, a direct link and precise mechanism for the association between talc use and ovarian cancer, do you think it had already been established prior to 2018?

A. I'm not a basic scientist. I'm not a biologist. What I look at in these studies for biological plausibility -- I don't know what biological proof is available. I didn't do a systematic total review of

the biology. And so I feel like I can't answer that question.

Q. So you are telling the Court it is not your area. Is that accurate? Is that a fair statement?

MS. PARFITT: Objection, your Honor.

MR. WILLIAMS: She was nodding in the affirmative.

THE COURT: I'll let the answer go.

Q. Let's go to some epidemiology.

Dr. McTiernan, for this litigation -- strike that.

Q. What I want to ask you now is a set of questions relating to the fit between the conclusions of a causal association between talc use and ovarian cancer as reflected in the studies that you cite in your report and the conclusions of those studies themselves. Do you have that topic in mind?

A. I do now, yes.

Q. For this litigation, you reviewed what you assessed to be relevant published epidemiological evidence concerning perineal use of talcum powder products and ovarian cancer. Right?

A. Yes.

Q. You reviewed 38 publications in scientific journals. Right?

A. Yes.
Q. Based on that review, it is your opinion that evidence of an association between genital use of talc powders and increased risk of ovarian cancer risk is, in your words, highly consistent. True?
A. I've looked at the data from those individual studies and at the meta-analyses, and from that I concluded what you just stated.
Q. Let's take a look at your report. It is Exhibit C 7 in your book, and for you, Dr. McTiernan, that would be in Volume 2.

MR. WILLIAMS: For your Honor it would be in Volume 3. And if we could go to page 64, and the heading "Consistency of Association," page 64. If we can pull that up.

Q. Do you see, Doctor, on that page, page 64, that you wrote:

"Across the case control and cohort studies, the association between use of talcum powder products and risk of ovarian cancer was highly consistent"?

A. Which page are you on?
Q. I'm on page 64, Dr. McTiernan.

Did I read that right? Was that your conclusion?

A. Yes.

Q. Let me ask you now to look at one of the studies you reviewed. It is called the Berge study. It is from 2018. It is in your notebook at Exhibit A 11.

MR. WILLIAMS: Your Honor, also in your first binder.

A. I have it.

Q. What we could do, Doctor, if at any time you want to see the study itself, of course, you may. You may also check me by looking at the screen to see if I am reading correctly.

Are you on Exhibit A 11, the Berge study?

A. Yes.

Q. The Berge study is one of the two recent meta-analyses that you consider to be excellent. Right?

A. Yes.

Q. The excellence of the Berge study, as you describe it, is actually one of the reasons why you say in your report that you did not conduct your own meta-analysis in this litigation. Correct?

A. Yes.

Q. Please look at the abstract on the cover page of the Berge 2018 paper. It is just below the list of authors. Do you see that right at the beginning?

A. The abstract, yes.

Q. When you read this study, the very first thing that you said, as follows:

"Some fecal studies suggest an association between genital use of talc powder and increased risk of ovarian cancer, but the evidence is not consistent."

That's what you read at first. Correct?

A. Yes.

Q. Let me ask you to focus on the last part of that statement where the authors described that the evidence suggesting an association between genital talc use and ovarian cancer was not consistent.

My question is: Did you disagree with that description of the evidence of the authors? Right.

A. Yes. I would like to add, most meta-analyses are systematic reviews, would state something along that line in order to justify publishing a meta-analysis. Otherwise, the journal might say, Why publish a meta-analysis? They have to give some justification.

Q. Are you now saying the authors of the Berge study did not in fact believe that the evidence of an association between genital talc use and ovarian cancer was not consistent? Are you testifying as to their state of mind?

A. I don't know what the state of mind was. I know this is a justification statement, a sort of justification that's pretty standard in a meta-analysis.
Q. As far as the Court is concerned, for purposes of assessing your reliance on this study, have we accurately set forth on the board your conclusion that the association was highly consistent and the Berge study conclusion that the evidence was not consistent?
A. This is what I stated, and I looked at the data such as in Figure 2 of their paper, which is very consistent to the forest plot here figure in the Berge paper, shows consistency across the studies in terms of the relative risk.
Q. When you review a study, it is your practice to always look at both the relative risk that is reported and statistical significance. Right?
A. When I look at a study I look at the relative risk and the statistical test the authors used to describe the relative risk.
Q. You always look at both the relative risk and the statistical significance. True or not true?
A. I always look at the relative risk and the results of whatever test they have done, whatever statistical testing they have done.

Q. Whatever statistical testing they have done you look at it?
A. Yes.
Q. And you consider that along with the reported relative risk. Right?
A. Yes.
Q. Statistical significance is what epidemiologists use that a likelihood of a relative risk or other estimate of risk did not just occur by chance. Correct?
A. That's not a full explanation of the statistical test, and I gave a wider explanation this morning, or the real explanation of what these mean. I think in my report, my expert report, I talked about chance, but what a p-Value really is is the probability that you will make an error if you reject the hypothesis of no association. The confidence interval, the 95 percent confidence interval is the likelihood of finding a relative risk in that range if you knew the universe of what a relative risk was. So it is a little more extensive than just something by chance.
Q. Statistical significance is what epidemiologists use to determine the likelihood that the relative risk or other estimate of risk did not just occur by chance. Correct?

A. I'm not sure what you are reading from.
Q. Your report.
A. I remember I put that in. What I explained this morning was the statistical reasoning, the statistical explanation of what the p-Value means.
Q. Let me ask you look at page 13 of your report, which is Exhibit C 7, the statistical analysis section, the fourth sentence there. You wrote:
"To determine the likelihood of these being true estimates of risk, rather than just occurring by chance, epidemiologists determine the statistical significance."
That's what you wrote. Right?
A. Yes.
Q. For the relative risk odds ratio and the hazard ratio estimates, epidemiologists calculate a confidence interval. Right?
A. Which shows the range of values the true risk estimate likely represents.
Q. And most commonly epidemiologists use a 95 percent confidence interval. Right?
A. The rest of the sentence, which means we are 95 percent sure a true relative risk or odds ratio lies within that interval.
Q. You wrote most commonly we -- you were referring

to was what was epidemiologists?
A. Yes.
Q. We epidemiologists use 95 percent confidence interval, which means we are 95 percent sure that a true relative risk or odds ratio lies within that envelope of numbers. Right?
A. Yes. It's consistent with what I described this morning.
Q. If a confidence interval -- and there is a lot of talk whether it includes one, so I want to make sure this is clear.

If a confidence interval includes the number 1.0, then you say the association between the exposure and the disease could be null. Correct?
A. Yes. That's consistent with the previous sentence that it could lie in that interval and that could be one if it includes that.

.
Q. "Null" means nonexistent. Right?
A. "Null" means a relative risk of one meaning no association. So, yes, it could lie within that interval. If the interval includes one, it could be one.
Q. It could be null. Correct?
A. It could be a relative risk of one.

Q. Relative risk of one means null?
A. It means no association.
Q. So "null," as you just said, there is no association between the exposure and the disease. True?
A. If the relative risk is one, the estimate is there is no association between exposure and the disease.
Q. Slightly different from what you wrote. What you write is:
"If a confidence includes the number 1.0, not that it was 1.0, or if it includes or passes over 1.0, you say that the association between the exposure and the disease could be null." Right?
A. With emphasis on the word "could," that the relative risk could be contained in that interval, if that interval includes one, it could be 1; but it could be any number between 1 and the top of the interval, and any number between 1 and the bottom of the interval. It doesn't tell us it's going to be 1, negative or positive. Somewhere in that interval. Again, it is a 95 percent probability estimate.
Q. As you said a moment ago, "null" means no association. Right?
A. If the relative risk fell on that, that would be

null. That's why I say if 1.0 is in the confidence interval, then it could be a null association, but it doesn't mean it is. It means it could.

Q. Where a confidence interval crosses 1.0, as an experienced epidemiologist, you say that the association was not seen. Right?

A. Can you cite to where I said this?

Q. I'm asking whether you believe that.

A. Maybe you can state it again then.

Q. Surely.

As an experienced epidemiologists, where confidence interval crosses 1.0, the association was not established, was not seen. Correct?

A. This is something that I've stated? Are you citing something?

Q. I'm asking you a flat out question, which I'm entitled to do. So my question is:

As an experienced epidemiologist, where confidence interval crosses 1.0, you say that an association was not seen, not established?

A. I think the real explanation of a confidence interval is that if it includes 1.0, it could be a null association. It could fall anywhere within the interval, and I think I'm saying the same thing -- go ahead.

Q. Have you completed your answer?
A. Yes.
Q. Let's go on to the Berge study. We've already talked about it a little bit. It is Exhibit A 11. I would like to go to Figure 2, which is the forest plot set forth in that study on page 8.
Figure 2 of the study identifies 27 different epidemiologic studies. I'm focusing on the case-control studies portion of that chart. Right, Doctor?
A. Yes.
Q. It identifies 27 epidemiologic studies, 24 which are retrospective case-control studies and three prospective cohort studies. Right?
A. Yes.
Q. Figure 2 shows the overall association between "ever" use of genital talc and the risk of ovarian cancer in the 27 studies. Correct?
A. Yes.
Q. The associations that are reported in this Figure 2 are estimated as relative risks, right, in the column over to the right?
A. Yes.
Q. And they are set forth with a 95 percent confidence interval. Right?

A. Yes.
Q. Let me ask you about one of the studies here so that we can understand how you applied concepts like statistical significance and confidence intervals in reaching your opinion.
Take a look at the reference to the Goodman study. That case-control study, like all of the other case-control studies, listed here was retrospective in design. Right?
A. Yes.
Q. Retrospective studies are backwards, looking where people are asked questions after they have contracted the disease, and they are asked to recall what they put on or in their bodies. Correct?
A. I would clarify, because the cases are the ones that have developed the disease, if it is a population-based study. The cases develop the disease and they asked about exposures; retrospectively, the controls have not have a disease, so they are asked about their exposure typically at a time when the cases had developed their disease. They usually are asked to remember back some time. I think your distinction sounded like everybody had a disease. That's what I was trying to clarify.
Q. The cases have disease; the controls do not.

Correct?
A. Correct.
Q. Both groups of people are asked the same questions; are they not?
A. Yes.
Q. Let's go back to the Goodman 2008 study. The relative risk for the Goodman 2008 study is 0.99. Do you see that?
A. Yes.
Q. The relative risk has a 95 percent confidence interval. Correct?
A. Yes.
Q. Now, to be clear, that confidence interval does not mean that the true relative risk is in fact 0.99 as opposed to, say, 0.80 or 1.0 or 1.2. Correct?
A. That's correct. The confidence interval does not tell you the relative risk. It just gives you a likely range.
Q. Instead, that confidence interval means that we can be sure, 95 percent sure that a true relative risk lies somewhere within the two numbers in the parenthesis. Correct?
A. I think the statisticians wouldn't talk so much about surety, but the rest of your statement is correct. It is an estimate that if you knew the

totality of the universe of evidence, that with 95 percent confidence it would fall within those intervals. It is still saying a very similar thing. It is just that word "surety" is not guaranteed from statistical tests.

Q. Looking at the high end of the confidence interval, the 1.4 number that would indicate genital talc use is potentially associated in the Goodman study with a 41 percent increased risk of developing ovarian cancer. Correct?

A. I think it is not talking about the individual study, the confidence interval. It is talking about the probability in a universe of what the relative risk could lie in. That's what I'm saying. In the Goodman study we know what the relative risk shows. In this case, it shows .99. So the confidence interval doesn't move the relative risk within a study. It talks about what the universe of information might be.

Q. Dr. McTiernan, did something in my question suggest to you I was saying the actual number was 0.99?

A. Maybe I misheard you. I thought you said in the Goodman study it would be such.

Q. We established a moment ago the 0.99 does not

mean that it is necessarily the correct number. Right?

A. In the universe. I don't remember saying that. Maybe I responded to something I didn't mean to. We know what the relative risk is in the Goodman study. We don't know what the true relative risk is in the universe of people with and without ovarian cancer.

Q. All I'm trying to establish is that the numbers that are within the parenthesis set forth a range, and it suggests in the Goodman study at least that the relative risk could reflect a 41 percent increase in the chances of getting ovarian cancer; but at the low end it could reflect a 30 percent decreased risk of getting ovarian cancer. Right?

A. I think as long as you are not suggesting that the Goodman study relative risk is different from what it is. It is talking about if you did the study again, another study, the universe of information, the relative risk could fall within that category given the results in that one study.

Q. Can I get a yes or no?

THE COURT: He's basing it on the Goodman study. He's not talking about what might happen again. He's trying to get an answer what those numbers reflect in this particular study for this

study. Isn't that right?

MR. WILLIAMS: That's correct.

THE COURT: You can answer that. Right?

THE WITNESS: It is difficult. My understanding of statistics is relative risk doesn't change based on what the confidence interval is. The relative risk is what it is. The confidence interval just tells us how we can infer this outside study, what the true relative risk might be. That's my understanding.

BY MR. WILLIAMS:

Q. Is that an understanding you've come to since the time you have prepared your report?

A. I've done more full reading, yes. The American Statistical Association has come out with some new position statements, new statements about --

MR. WILLIAMS: Can I cut her off, your Honor?

THE COURT: You don't have to tell us what it is. All he asked is, and he said yes.

Q. You have a different opinion now than at the time you wrote your report. Yes or no?

A. It is more fully informed.

Q. Because the confidence interval in Goodman 2008 includes the number 1, that means that the association reported in that study could be null. Correct?

A. I would say the true relative risk could be null.
Q. You cannot rule out the possibility that there is no association between ever genital talc use and ovarian cancer in the Goodman study because of the results that were reflected here which passed through 1.0. Right?
A. You are saying you cannot rule out no association between genital talc use and risk of ovarian cancer?
Q. Precisely.
A. To that I would say yes.
Q. Let's take a look at the entire Figure 2 on this page. It consists of 24-case-control studies, and then there are the three cohort studies down below. Right?
A. Yes.
Q. Looking at the top of the forest plot Figure 2, do you see the Hartge 1983-case-control study, second one down from the top. Do you see that?
A. Yes.
Q. That study as well includes the number 1.0 meaning the low end of the interval is below 1.0. Right?
A. Yes.

Q. If we can go through this quickly. The same is true for Whittemore, 1983, right, the confidence interval falls below 1.0?
A. Yes.
Q. Both 1999?
A. Yes.
Q. Harlow and Weiss, 1989?
A. Yes.
Q. Chen, 1992?
A. Yes.
Q. Rosenblatt, 1992?
A. Yes.
Q. Tzonou, 1993?
A. Yes.
Q. Godard, 1998?
A. Yes.
Q. Wong, 1999?
A. Yes.
Q. Goodman, 2008, that's what we just discussed. Right?
A. Yes.
Q. Merritt, 2008?
A. Yes.
Q. And Rosenblatt 2011?
A. Yes.

Q. So if we just looked at those case-control studies that had a confidence interval that crosses over 1, there are 12 of them, 12 of the 24. Correct?
A. Yes.
Q. Half of the case-control studies in the Berge 2018 meta-analysis have confidence intervals that include the number 1.0. Right?
A. Yes.
Q. That means that there are case-control studies, the results of which are not statistically significant. Correct?
A. If we look at the sample size, which I talked about this morning, the smaller studies tend to have very small -- tend to have wide confidence intervals. So, yes, all of these confidence intervals include 1.
Q. And that means there are 12 that are not statistically significant. Correct?
A. If you are using the term "statistically significant" to indicate that the confidence interval includes 1, the answer is yes.
Q. Let me ask you to look at your red binder at your deposition testimony, and I'll direct you to page 245. I'm directing your attention to page 245 through line 24, to page 246, line 1.
"QUESTION: And that means that there are 12

that are not statistically significant. Correct?

"ANSWER: Yes.

Was that your answer then?

A. Yes.

Q. The overall association in half of the studies in Berge could be null. Correct?

A. Yes.

Q. There in fact is no association between genital talcum powder use and ovarian cancer in those case-control studies. Right?

A. No, I wouldn't say that.

Q. If the confidence interval includes the number 1.0, then we can say that the association between the exposure and the disease could be null. Correct?

A. It could be null. I think your next statement was that there was no association. So that's not the same as could be no association. I think you asked me that there was no association. So there is a difference between was no association and could be no association.

Q. We went to the case-control retrospective studies, but we haven't discussed the prospective studies, so let's do that now.

You did a Bradford Hill analysis here, and you put up those factors on the board. Right?

A. Yes.
Q. Let's take out what we have marked as Exhibit A 63, which is a Bradford Hill presentation. If you turn to page 1 of Exhibit A 63, do you recognize as the address by Sir Bradford Austin Hill that identifies what has become known in your field as the Bradford Hill factors or criteria?
A. Yes.
Q. Please turn to page 2 of Exhibit A 63, the right-hand column, first full paragraph. That is Sir Bradford Hill's description of consistency. Right?
A. Yes.
Q. He writes:

"Next on my list of features to be specially considered I would place the consistency of the observed association. Has it be repeatedly observed by different persons in different places, circumstances, and times?"

Right?

A. Yes.
Q. Now, please turn to page 4 and look at the left column, the very top paragraph that carries over from the previous page. There is a sentence there that begins with:

"I myself would put a good deal of weight

upon:

A. Can you please tell me where you are. My page 4 of the Bradford Hill first paragraph starts "A particular occupation" --

Q. Can you see the page in the upper right-hand corner, it should have 297 on it?

A. Okay.

Q. Left-hand column, first sentence:

"I would myself put a good deal of weight upon similar results reached in quite different ways, for example, prospectively and retrospectively."

Right?

A. Yes.

Q. He is saying, I think there should be particular weight if there's consistency with retrospective studies or forward looking studies.

Right?

A. I don't see the word "should." I see he said he would put a good deal of weight on similar results reached in quite different ways, for example, prospectively and retrospectively.

Q. In your opinion, the association between the use of talcum powder products and the risk of ovarian cancer is consistent across study designs, specifically across case-control studies and cohort

studies?
A. As I looked at the data this morning on the forest plot, I saw consistency that most of the studies were to the right of the line, most were in the positive direction, the relative risk.
Q. We put up your report earlier under the second heading "consistency." Do I need to put that up again? It said:
"Across the case-control and cohort studies, the association between the use of talcum powder products and risk of ovarian cancer was highly consistent."
Do you remember? Do you recall that?
A. Yes.
Q. The idea of a prospective cohort study, is that people are asked what they do and what they put on, and in their bodies right now when they are healthy, and then they are followed along? Correct?
A. Yes.
Q. You reviewed the Gertig 2000 study reporting on the Nurses' Health Study cohort. Right?
A. Yes.
Q. You reviewed the Gates 2008 paper also relating to the Nurses' Health Study. Right?
A. Part of the 2008 was Nurses', part was a

case-control study.

Q. You reviewed it?

A. Yes.

Q. You reviewed Gates 2010 also relating to the Nurses' Health Study. Right?

A. Yes.

Q. You reviewed the Houghton 2014 study?

A. Yes.

Q. That report relates to the Women's Health Initiative on which you worked. Right?

A. Yes.

Q. You also reviewed the Gonzalez 2016 study reporting on the Sister Study cohort. Right?

A. Yes.

Q. Those are five papers reporting results from three prospective cohort studies that you reviewed. Right?

A. Yes.

Q. True or not true: Every single one of the prospective cohort studies that you reviewed in forming your opinions in this case reports an overall risk estimate for genital talc use and ovarian cancer that has a confidence interval crossing 1.0?

A. Yes. Usually I talk about the relative risk and then I talk about the confidence interval. I don't

usually talk about just one, but, yes.
Q. I'm not asking you what you talk about. Is the answer to my question yes?
A. As an epidemiologist, I don't just talk about confidence intervals and about p-Values. I talk about relative risk for consistency.
THE COURT: When he asks you a question, respond to the question that he has.
THE WITNESS: Okay.
THE COURT: He is only focusing on that for the moment. I know we've heard your testimony about how you viewed it all day tomorrow, so we understand that.
MR. WILLIAMS: Thank you, your Honor.
Q. In 100 percent of the prospective cohort studies there was no overall association found between genital talc use and ovarian cancer. Correct?
A. I would have to disagree with that.
Q. If confidence interval includes the number 1, then we say the association between the exposure and the disease could be null. Correct?
A. I agree with that.
Q. In 100 percent of the prospective cohort studies you could not rule out the possibility that the true relative risk in each and every one of the prospective

studies is null. Correct?
A. I cannot -- say it again. Just repeat it. I think it's close to what I understand, but, please.
Q. You cannot rule out the possibility that the true relative risk in each and every one of the prospective cohort studies is null?
A. Correct.
Q. "Null" means zero, right, nonexistent?
A. It means non-association or a relative risk of 1.
Q. You cannot identify any prospective cohort study concluding that there was a statistically significant overall association between talc use and ovarian cancer. True?
A. True.
Q. It is your opinion an association between genital talc use and ovarian cancer risk is highly consistent across case-control and cohort studies across those study designs. That's your opinion. Right?
A. Yes.
Q. One of the reasons that you did not perform your own meta-analysis in this case was because you believed the recently published Penninkilampi and Berge meta-analyses were in your words excellent

studies. Right?
A. Yes.
Q. Both of those studies included a meta-analysis that stratified or broke-out study design, right? They described cohorts and described case-controls separately. Correct?
A. Yes.
Q. Both Penninkilampi and Berge included an odds ratio for the combined retrospective and case-control studies on the one hand and a separate odds ratio for the combined prospective cohort studies. Right?
A. I want to look at both of them. Berge, I believe so; and Penninkilampi, I would like to look at again.
Q. This is A 109, and I'm referring to page 6, Table II. That is a summary of pooled effect sizes in a subgroup analysis. Right, Doctor?
A. Yes.
Q. And it shows an overall association between any perineal talc use and ovarian cancer stratified by study design estimated as an odds ratio. Right?
A. Yes.
Q. And looking at the stratified analysis in Table No. 2, the combined odds ratio for the case-control study was 1.35 with a 95 percent confidence interval

of 1.27 to 1.43. Do you see that?
A. Yes.
Q. The study also shows the combined odds ratio for the cohort studies. Right?
A. Yes.
Q. The three cohort studies are listed there. Correct?
A. Yes.
Q. And in that analysis that you rely upon for your opinions, at the combined odds ratio for the cohort studies was 1.06 with a 95 percent confidence interval of 0.90. Right?
A. Confidence interval, that was the lower?
Q. Yes. It is right on the board there. Do you see any perineal use?
A. I didn't hear the upper limit.
Q. The upper limit is 1.25. Do you see that?
A. Yes.
Q. This includes the null, which is the possibility that there is in fact no association at all between genital talc use and ovarian cancer. Right?
A. Yes.
Q. Let's go to the Berge study. That's Exhibit A 11. Do you have that in front of you?
A. Yes.

Q. I direct your attention to Figure 2 on page 8. If we pull out that chart, if we could look at the bottom, a subtotal, and do you see the subtotal -- that's the wrong one -- the subtotal for the cohort studies is 1.02. We can agree that is an extraordinarily low point estimate?
A. It's low, yes.
Q. And the confidence interval is 0.87 on the low end and the upper end is 1.20. Right?
A. 0.85.
Q. 0.85. And the upper limit is 1.20. Did I read that right?
A. Yes.
Q. So the same confidence interval indicates that a true combined risk estimate for the cohorts within that range is as high as a 20 percent increased risk and as low as a 15 percent decreased risk. Right?
A. Again, you are talking about -- the way I read this is that the relative risk, the meta-analysis for those three cohorts is a 1.02 relative risk with a confidence interval that we just mentioned. So that indicates a confidence interval -- indicates what the relative risk may truly be in the universe of cohort studies. That's what I'm trying to say. I'm not sure that confidence interval means that those three cohort

studies, their relative risk would be in that interval, and you could already see the relative risk for one of them falls outside of it.

That's why I'm saying when I look at a confidence interval it means this is what a true relative risk could fall within.

Q. You would agree that the confidence interval at the upper end would indicate a 20 percent increased risk. Right?

A. Yes.

Q. And equally true, based on the confidence interval reported on page 7 of this exhibit, that the relative risk could be as low as 0.85. Correct?

A. Yes.

Q. Let me ask you some questions about power calculation. We have been talking about the cohort studies, and I understand you have some criticisms of the cohort studies. Is that fair?

A. There are strengths and limitations of both cohort and case-control studies.

Q. One reason that you have stated for the lack of statistical significance in the cohort studies is that the number of cases, the sample size of cancer cases in those studies is too low. Right?

A. Yes.

Q. You are distinguishing between the total sample size on the one hand meaning every woman in the study versus those women in the study who have cancer. Right?
A. The power to determine the relative risk depends on the number of cases.
Q. What is important for your analysis in terms of the sample size is the number of cancer cases. Correct?
A. Yes.
Q. You believe that the number of cancer cases affects the statistical power of these cohort studies we have been discussing. Right?
A. Individually, yes.
MR. WILLIAMS: This is Dr. McTiernan's testimony at page 215, lines 16, through the same page, line 18:
Q. (Reading.)
"QUESTION: Do you believe that the number of cases affects the statistical power of the studies"?
Q. Line 16.
(Reading.)
"ANSWER: Yes.
"QUESTION: You believe the number of cases affects the statistical power of the studies?

"ANSWER: Yes."

Now, you performed your own power calculation to determine the sample size that you believe is required for a study to have sufficient power to detect a statistically significant association. Right?

A. Yes.

Q. And one of the reasons why you believe that the meta-analyses that have been done in the last, say, five years are helpful is that they are able to combine the number of cancer cases. True?

A. Because they have additional power because they have many more cases.

Q. And the way that you get many more cases is by combining the number of cancer cases among the studies. Correct?

A. My understanding is meta-analyses' power calculations don't just add together numbers. I haven't done the power calculations myself, but it is not the same as adding. But, conceptually, more cases provides more power. I just can't say that you would apply the same power calculation to a meta-analysis and then immediately get the right answer.

Q. Let's get the record clear.

You have testified that you personally have

performed what is known as a power calculation to determine the sample size that you believe is required for a study. Correct?

A. An individual study, yes.

Q. And you place particular importance on that because you are focused on the number of cancer cases. Right?

A. Yes, in individual studies particularly.

Q. Your calculation, the one in your litigation report, you defined "good power" as power sufficient to detect a relative risk of 1.3 with the statistical significance of 0.05. Right?

A. Yes.

Q. Based on your calculation, you concluded that you have good power the number of cases would need to be 931. Correct?

A. Yes.

Q. None of the cohort or case-control studies that you reviewed had sample sizes that large. Right?

A. Correct -- sorry. None of the case-control or cohort?

Q. Correct.

A. I think some of the case-control studies do have sample sizes that big.

Q. Almost none of the case-control and cohort

studies?
A. I would need to look at the numbers. There are several that have more than 931, but it is not the majority.
Q. For that reason it was your opinion the evaluation of the meta-analysis and the pooled analyses with their larger sample sizes is critical to understanding the state of the evidence. Right?
A. Yes.
Q. And you wrote in your report on page 48, Exhibit C 7, page 48, the meta-analysis section, bottom half, after that hyperlink:
"Lack of statistical significance found in the various studies is likely due to their small sample sizes. For this reason, evaluation of the meta-analysis and pooled analysis with their larger sample sizes is critical to understanding the state of epidemiological evidence linking use of talcum powder products to risk of ovarian cancer."
Correct?
A. Yes.
Q. These meta-analyses, they look at the number of cases across the cases that are part of the meta-analysis. Right?
A. Say it again.

Q. The meta-analyses look at -- the meta-analyses and the pooled analyses, with their larger sample sizes, derive their larger sample sizes by taking the sample sizes from multiple other studies and putting them together. Right?

A. Yes. In terms of power, however, it is not as simple as adding them up together. You get more power by doing the meta-analysis, but it is a different power calculation to my knowledge. Doing a meta-analysis corrects for much of the lack of numbers in individual studies, but it doesn't completely correct it from my understanding because of the variability in the individual studies. That's why I don't want to say you immediately have completely enough power by adding studies together. I know there are power calculations that are done specifically for meta-analyses.

Q. The point that you were making in performing your power calculation -- let me stop for a second. You performed a power calculation, did you not?

A. I did to consider for individual studies.

Q. The point you were making in performing your power calculation was that with meta-analysis, with their larger combined sample sizes, that could be used to overcome the lack of statistical power. True?

A. The word "could" is key here, yes.
Q. Did you understand me to be saying "could"?
A. I thought I heard the word "could," that it could overcome the lack of power in individual studies -- maybe you could repeat what you said.
Q. I'll ask the question again:

The point that you were making in performing your power calculation was that meta-analyses with their larger combined sample sizes can be used to overcome that lack of statistical power. Is that true?

A. It can correct for much of the problems. It just can't completely correct for individual studies' lack of power, to my understanding.

MR. WILLIAMS: Permission to read, your Honor --

THE COURT: Yes.

MR. WILLIAMS: -- from the Doctor's deposition at page 217, lines 12 through 16.

(Reading.)

"QUESTION: The point you were making in performing your power calculation was that meta-analyses, with their larger combined sample sizes, can be used to overcome that lack of statistical power. Is that true?

"ANSWER: Yes."

Q. Now, Doctor, I would like you to take a look at the Berge 2018 meta-analysis, which is Exhibit A 11 and I would ask you to turn to page 7.

Take a look at the paragraph starting at the top of the right-hand column there, halfway down that paragraph starting with, "It should be noted." Are you with me?

A. Yes.

Q. The Berge study wrote:

"It should be noted that the cohort studies included in the meta-analysis comprised a total of 429 cases of ovarian cancer cases exposed to genital talc and 943 unexposed cases. The statistical power of the meta-analysis of these cohort studies to detect an RR of 1.25 similar to the result of the meta-analysis of case-control studies was 0.99. Thus, low power of case-control studies cannot be invoked as explanation of the heterogeneity of the results."

Is that what they said?

A. Yes.

Q. The Berge study is one of the two meta-analyses that you said is an excellent study. Right?

A. I'm just noting the 429 cases does not look correct for the cohort studies.

Q. I'm asking you a question, Doctor.

The Berge study is one of the two meta-analyses that you said is an excellent study. Correct?

A. Yes.

Q. And what they list here on page 7 of the Berge study is 429 cases or exposed cases of ovarian cancer and 943 unexposed ovarian cancer cases. Right?

A. Yes. I misread it. That's what they say.

Q. If you add those two numbers together, you get over 3900 actual cancer cases. Right?

A. Yes.

Q. Now, in your report, based on your power calculation, you concluded that the minimum number of cases would need to be 931. Correct?

A. Yes.

Q. Can we agree 1372 is more than 931?

A. Yes. But my power calculation was for an individual study. However, they have done a power calculation, and I assume they have done it for meta-analysis. So I would trust their statement that the power was .99 rather than extrapolating from my power calculation which was for one study.

Q. This Berge study that you say is an excellent study sets forth a power calculation that suggests

that lack of power should not be a valid criticism of the cohort studies. Correct?

A. Given their power calculation.

Q. And you have no reason, as you said a moment ago, to doubt that calculation. Correct?

A. Correct.

Q. Let me ask some questions about epidemiology and some basic principles.

You mentioned on direct examination that you have worked on comprehensive written reports for the U.S. Government in your career?

A. Yes.

Q. And in the section of your report entitled "Overall Approach," -- if we can pull that up, it is page 7 -- you had an overall section in your report, and you drew upon your years of experience, and you wrote that for purposes of your work here you drew upon that experience with synthesizing and interpreting large numbers of epidemiologic studies for comprehensive reports. Right?

Let me draw your attention to this particular part.

A. It says, page 9 --

THE COURT: He has it up on the screen.

THE WITNESS: I see it.

Q. (Reading.)

"Among the different engagements that you had is work with the World Health Organization International Agency for research on cancer, IARC, and the World Cancer Research Fund" -- correct?

A. Yes.

Q. (Continuing.)

-- "for the World Cancer Research Fund, you are a member of the advisory panel of experts that guides interpretation of meta-analyses and does systematic reviews of nutrition, physical activity, obesity and risk factors for many cancers, including ovarian cancer."

Is that true?

A. My work on that panel is completed. I'm on an interim panel now.

Q. As of the time I took your deposition, you were still on that panel. Correct?

A. I might have stated it had recently come to an end. I believe I stated that in the deposition.

Q. In your binder, take a look at Exhibit A 153.

MR. WILLIAMS: This is the World Cancer Research Fund, Judge, the evidence report.

Q. Do you have that in front of you?

A. 153 in Binder 1, I don't see it.

(Pause.)

Q. Do you have that in front of you?

A. Yes.

Q. Now, the continuous research project that you did for 2018, the purpose of it was to consider scientific research from around the world, and to evaluate that literature and make findings based on it. Is that accurate?

A. Yes.

Q. The third paragraph explains on the page that we have on the board, which is, I think, page 5 of the document, explains why the CUP does all of its work and it says:

"Through this process the CUP ensures that everyone including policymakers, health professionals, and members of the public has access to the most up-to-date information on how to reduce the risk of developing cancer."

(Pause.)

Do you have that in front of you, Doctor?

A. Yes, I do.

Q. There is a portion of this report where you and your colleagues explained how to cite the document. It is on page 5. It is another section on the same page, how to cite the third expert report. Correct?

A. Yes.
Q. So the idea is, this is an actual report that could be cited, and you explain how it could be cited if one chose to do so. Correct?
A. Yes.
Q. And as of last year, in 2018, you were a member of what was called the "Advisory Panel of Experts For the World Cancer Research Fund." Right?
A. Yes.
Q. This exhibit, A 153, was published by that organization at the time you served as a panelist for the organization in 2018. Correct?
A. This exhibit was published at that time. Is that what you are saying?
Q. I'm saying this exhibit was publish by the WCRF at the time you served as a panelist for that organization in 2018?
A. Yes.
Q. 2018 was two years after you were retained by plaintiffs' counsel. Correct?
A. Yes.
Q. Let's turn to page 31.
You were acknowledged here in the left-hand column at the bottom, and you appear in the photograph that appears on that page. Right?

A. Yes.
Q. The expert advisory panel that you were on, guided interpretation of meta-analyses and systematic reviews on those topics we discussed, nutrition, physical activity, obesity, and risk for many cancers -- right?
A. For those variables specifically, yes.
Q. Including ovarian cancer. Correct?
A. Yes.
Q. Please turn to page 8 of the exhibit. The last paragraph is on study design. That paragraph on study design starts by saying:
"Each study design has its advantages and limitations" -- you said that here today?
A. Yes.
Q. You agree with the WCRF there are good things and bad things about any study. Correct?
A. There are good things and bad things --
Q. Any study type?
A. Yes.
Q. True or not true:
"The hierarchy of epidemiological evidence places cohort studies above case-control studies?"
A. I would note that the top of this section -- this is a box issues concerning interpretation of

epidemiologic tests.

It states:

"Interpretation of epidemiologic evidence on identity, nutrition, and physical activity, and the risk of cancer is complex, and expert judgment is essential. General considerations that need to be taken into account when evidence is assembled and assessed include the following" -- and then there are six bullet points, and I believe Mr. Williams is talking about the bottom bullet point under that heading."

Q. True or not true:

"You and your colleagues published a report that says: The hierarchy of epidemiological evidence places cohort studies above case-control studies with ecological studies and case reports at the bottom. There are merits in considering a number of different study designs. Cohort studies are likely to be the main source of evidence owing to the long latent period for cancer to develop and also to their prospective design. However, in some circumstances case-control studies and ecological studies may also make a useful contribution to the evidence. See Section 7."

Did I read that correctly?

A. Yes. And that's referring to the diet, physical activity and nutrition variables it mentions at the top.

Q. Did I read it correctly?

A. Yes.

Q. If you look at the last paragraph in the left-hand column -- and I would like to turn to page 22 now -- the last paragraph in the left-hand column says:

"The work from the 2007 second expert report was used as a starting point." Correct?

A. Yes.

Q. The acronym SLR in the continuous update project refers to systematic literature review. Correct?

A. Yes.

Q. Continuing on page 22 of the update project report, it says:

"The first stage of the SLRs was a comprehensive search using standardized search strategy -- a standardized search strategy for the scientific literature for randomized controlled trials and cohort studies published since 2006 using MedLine."

Right?

A. Yes.

Q. And it goes on to explain:

"Because case-control studies are particularly prone to recall and other bias, they were not routinely reviewed. However, if there were no or very few RCTs or cohort studies, they were included. That was the methodology you employed."

Right?

A. This is what they stated at the last meeting I was in. They stated that they do include case-control in the search. So here it's clear what they say about review. But the search part is not completely correct.

MR. WILLIAMS: Move to strike as nonresponsive.

THE COURT: His question was, Is that what the report says?

THE WITNESS: Then yes.

BY MR. WILLIAMS:

Q. For the analysis that you did in this litigation, you reviewed prospective cohort studies. Right?

A. You are talking about the current -- the current litigation?

Q. Yes. I'm jumping forward to today.

A. Yes.

Q. The work you have done in this matter you reviewed prospective cohort studies. Right?
A. Yes.
Q. None of those studies concluded that there was a statistically significant overall association between talc use and ovarian cancer. Right?
A. Their conclusion, correct.
Q. Would you agree with me that if you had only looked at the cohort studies in this case, like you did as part of the expert advisory panel for the World Cancer Research Fund, you would not have been able to opine talcum powder causes ovarian cancer?
A. If I didn't look at the totality of evidence, I might have come up with a different answer.
Q. My question was a little different. My question was: If you had only looked at the cohort studies, all of which found no statistically significant association, you would not have been able to come to a conclusion that talc actually causes ovarian cancer. Correct?
A. I think I can't assume what I would come up with. I know one of the cohort studies did have a positive association for serous cancer. I haven't considered -- to answer your question, I haven't considered what my conclusion would have been if I

looked only at a subset of studies.
Q. In your last answer, you mentioned one of the studies found a positive association for serous invasive ovarian cancer. You just said that, right?
A. Yes.
Q. You are referring to Gertig 2000. Right?
A. Yes.
Q. You are aware later Gertig studies -- strike that.
Later studies that followed the same women along farther in time through 2006, 2008, 2010 did not find a statistically significant positive association between use of talc and serous invasive ovarian cancer. Correct?
A. They used a different comparison. It is difficult to say what they would have found if they used the same comparison. So they did not. They compared "ever" uses plus "once-a-week" users to "greater" users. I don't know what the relative risk would have looked like had they done the same comparison as the first paper.
Q. Let's unpack that. You do not know what the relative risk would have looked like had they used the same criteria, is what you are saying. Right?
A. Yes.

Q. But you also do not know it would have been different than the finding that they made in 2010. Correct?
A. Correct.
Q. You do not deny that in 2010, when the women had been followed for a longer period of time, the positive association for serous invasive ovarian cancer fell away and there was no statistically significant association. True?
A. There was no association in their data as they presented it.
MR. WILLIAMS: Your Honor, is this a good time for a break?
THE COURT: Absolutely. Thank you.
THE DEPUTY CLERK: All rise.
(Recess is taken.)
(Continued on the next page.)
///

THE DEPUTY CLERK: All rise.

THE COURT: Thank you.

Anne McTiernan, resumed.

CROSS-EXAMINATION

BY MR. WILLIAMS:

Q. Good afternoon, Dr. McTiernan.

In your opinion, if risk for disease increases with the amount of exposure, the likelihood of a causal relationship goes up. Right?

A. Yes.

Q. That is essentially the concept of dose-response. Right?

A. Yes.

Q. You reviewed the Terry 2013 study, and we referred to that earlier today, which is Exhibit A 31. Do you have that in front of you?

A. Yes.

Q. In your opinion, the Terry 2013 pooled analysis provides strong evidence that perineal use of talcum powder causes ovarian cancer. Right?

A. I'm sorry. You said 831 for the reference, yes.

Q. I said A 139. We have it up on the board.

It is your opinion that that study provides

strong evidence that perineal talcum powder causes ovarian cancer. Right?

A. Yes.

Q. In your report Exhibit C 7, page 55 of the report, you wrote:

"The Terry, et al, pooled analysis provides strong evidence that perineal talcum powder product use causes ovarian cancer. Strong here does not pertain to the size of the odds ratio/relative risk. Rather, it refers to the fact that the number of cases included was larger than any previous study. The eight-case-control studies included showed similar effect sizes for association of genital powder use and ovarian cancer risk consistency."

This the part I want to focus on.

"The dose-response effect was clear and there were enough numbers of cases to determine effects on subtypes of ovarian cancer."

I read that right?

A. Yes.

Q. The opinion is based in part on your conclusion that the study showed a clear dose-response effect. Right?

A. Yes.

Q. Terry 2013 pooled eight case control studies.

Correct?
A. Yes.
Q. The data from five of those case-control studies were previously published -- meaning published in a different paper -- before they were mentioned in Terry 2013's pooled analysis. Correct?
A. Yes.
Q. And you wrote that in your report. You made that precise statement that the data from five of the studies were previously published, but that three were not previously published?
Do you remember that?
A. Yes.
Q. In this litigation -- and I mean in your report for this litigation -- you define a pooled analysis -- and this is page 22 of your report, Exhibit C 7, first full paragraph, first sentence -- you defined a pooled analysis as "a type of meta-analysis where original individual level data from various published and/or unpublished epidemiological studies are combined and reanalyzed."
Did I read that right?
A. Yes.
Q. Now, Terry 2013, which included previously unpublished talc data from three case control studies

fits the description of a pooled analysis in your litigation report here. Right?
A. Yes.
Q. So in relying on Terry 2013 as part of the science relating to use of talcum powder and risk of ovarian cancer, you relied on the data from those previously unpublished studies. Correct?
A. I relied on the data on the eight studies that included those three unpublished, yes.
Q. Now, let me pull up your report again. There is one citation there, citation No. 39. There is one and only one citation there. Correct? There is just citation for that proposition. Correct?
A. I'm trying to find my report.
Q. I'll represent to you that is the Terry study. Will you take my representation?
A. Okay.
Q. I would like to pull up your definition again of what a pooled analysis is.
MR. WILLIAMS: If we could put that up, page 22, C-7.
Q. Looking at the first two sentences there, you cannot point us to any referenced material that you have reviewed anywhere that describes a pooled analysis, using the words that you set forth here in

your report. Correct?
A. I'm not sure. There have been methods, papers written about pooled analyses. I'm not sure if they -- I'm not sure if they use these particular concepts.
Q. You wrote these two sentences here on page 24 of your report, correct, defining a pooled analysis?
A. It is in my report, yes.
Q. My question was a simple one; it was -- can you point the Court to any reference material that you have reviewed that describes a pooled analysis, using those words, with particular reference to published and/or unpublished epidemiological studies?
A. I know that I did not cite -- I did not cite Friedenreich 1993 as a description of pooled analyses. And I did not cite that in my report. I did use World Cancer Research Fund methods description in my report that's cited not here but cited overall in the report.
Q. Now, the Friedenreich paper 1993 is not referenced in your report?
A. It is not in my report.
Q. Let's talk about the World Cancer Research Fund document. It has already been discussed, Exhibit A 153, the "judging the evidence" report that you, your colleagues published in 2018, just last year.

A. But this report --
Q. There is no question pending.
Let's take it one step at a time.
Please turn to page 12 of Exhibit 153. Do you have that in hand.
A. On the -- yes.
Q. On the right-hand side of that page, do you see a definition of "pooled analysis" that is contained in the report? Do you see that?
A. Yes.
Q. Here you and your colleagues wrote:
"Pooled analysis is a type of meta-analysis in which original individual level data from various published epidemiological studies of a similar type, usually prospective cohort studies, are combined and reanalyzed."
Did I read that right?
A. Yes.
Q. It goes on and says:
"The combination of data from multiple studies creates a larger data set and increased statistical power."
Right?
A. Yes.
Q. The sentence also includes the phrase "of a

similar type, usually prospective cohort studies."

Do you see that?

A. Yes.

Q. So in the World Cancer Research Fund definition of a "pooled analysis," it references studies of a similar type, usually prospective cohort studies. Right?

A. Yes, it says that.

Q. Let's look at the version of your report.

In your report you wrote:

"Pooled analysis is the type of meta-analysis where original individual level data from various published and/or unpublished epidemiological studies. The definition in the World Cancer Research Fund does not say and/or unpublished."

Can we agree?

A. Yes.

Q. And your definition in your report at page 22 does not include the language that was included in the World Cancer Research Fund of a similar type, usually prospective cohort studies. Right?

A. Correct.

Q. Now, did the members of the World Cancer Research Fund have your report at the time this study came out? This paper from WCRF came out in 2018.

A. No.
Q. You did have the WCRF paper at the time you wrote your report for this matter. Right?
A. Yes.
Q. And you personally typed up your paper. Correct?
A. Yes.
Q. And when you typed it up, you added "and/or unpublished." Right?
A. I included those words, yes.
Q. And you took out a similar type, usually prospective cohort studies. Right?
A. Those words are not in my version, yes.
Q. The reason that you added "and/or unpublished" was that you knew that the study that you were relying upon with its pooled analysis included data from three studies that were unpublished. Right?
A. I don't think so. Pooled analyses, they're pooling projects that begin with no published studies. The pooled analysis I collaborated in began with us providing data to investigators, some of which had been published, some not. The NCI funds many pooling projects. Pooling projects can be with randomized control trials. It is very common. Pooling projects have been with case control studies. One of my

pooling projects was case-control studies. One of my projects was a pooling study of randomized trials. My statement in the report needed to be more general than what WCRF indicated.

Q. Let's go to your report C-7, page 8, first full paragraph, your description of the Terry pooled analysis. What you wrote in your report was the pooled analysis which included data from five previously published and three unpublished case-control studies.

And you went on."

That's what you wrote?

A. Yes.

Q. And the reason you took this part out in the description of a pooled analysis -- and by "this part," I'm referring to the words "of a similar type usually prospective cohort studies," is that you knew if the definition of pooled analysis that you and your colleagues used for the WCRF had been applied to this case, it would have focused the Court on the prospective cohort studies, none of which has found an association between talc use and ovarian cancer.

Is that true?

A. No.

Q. Do you deny you added the words "and/or

unpublished" and removed the words "of a similar type usually prospective cohort studies" when you wrote the definition of "pooled analysis" in your report?

A. I agree many of the words are the same. This is an epidemiologic concept. If I were to write what the WCRF definition says in some other context, it would not be correct because it is not true that only cohort studies are done for pooled analyses.

Pooled analyses -- as I mentioned, my first pooled analysis was years before 2016. It was 20 years before, which was case-control studies. My second pooled analysis was a couple of years before 2016. That was randomized control trials. I also participated in cohort study pooled analysis, and published from that. And so it is a very general type of epidemiology. It's not limited to cohort studies.

So it would be incorrect for me to say "usually prospective cohort studies" because that is not the case. And for published and/or unpublished, I didn't want to leave a statement that says "original individual data from published epidemiologic studies" because that is not the case. In some pooled projects there will be published and unpublished data, and that has been true in my studies and many other pooled projects.

Q. Did you understand my last question to be suggesting your definition of a pooled analysis from the WCRF paper said only prospective studies?

I read it accurately and said "usually prospective cohort studies," I read that correctly; didn't I?

A. Even the word --

Q. One question at a time.

Did I read it correctly or not? I said "usually and not only." Right?

A. It sounds like that's what you said, yes.

Q. My point is, if you had focused your attention on the prospective studies for purposes of this matter, then the definition that you and your colleagues used for the WCRF would have hurt the plaintiffs in this case; would it not?

MS. PARFITT: I object.

MR. WILLIAMS: Hurt the plaintiffs' position.

THE COURT: Thank you.

BY MR. WILLIAMS:

Q. Do you understand my question?

A. My purpose in writing it was to be complete about the methodology, and it didn't occur to me what would help one side or the other when I wrote my methodology.

Q. In both definitions, the one in the WCRF paper and in your report here, the next sentence appears word-for-word. Right? The combination of data from multiple studies creates a larger data set and increased statistical power. Correct?
A. Yes.
Q. Let me ask you some questions on dose-response, please.
On the question of dose-response, -- that is, whether the studies you reviewed showed or did not show an increasing risk of ovarian cancer from increased talc use -- you agree that not all of the studies on that list of the 28 studies, looked into that question. Right?
A. Correct.
Q. Of the studies that did look into dose-response, not all of those studies found a dose-response. Right?
A. Correct.
Q. Some purported to find a trend; some did not. True?
A. Correct.
Q. So just on that question, the question of whether or not the studies that looked at dose-response found a trend, the studies reached

inconsistent results. True or not. True?
A. True.
Q. Your opinion in this litigation is that cumulative exposure, meaning frequency of genital talc use, how often one uses it, and duration or times duration, meaning years of talc use is the optimal metric of dose-response effects. Right?
A. Yes.
Q. You agree, though, not all studies examining the cumulative dose-response found a trend or a dose-response. Correct?
A. When you say "trend," maybe you can define that.
Q. Sure.
For purposes of my question, please focus on those studies that examined what you call cumulative dose-response, meaning cumulative use, frequency times duration. Do you have that subset in mind?
A. Yes.
Q. With those studies that did use that type of calculation, some purported to find a dose-response and some did not. Right?
A. Correct.
Q. So on that question, the question of whether or not the studies that looked at a cumulative use found a dose-response, on that question, the studies reached

inconsistent results. Right?
A. Correct.
Q. Let's go to Terry A 139. I'll direct your attention to page 8, the right-hand column, first full paragraph about midway down. I'm looking for the sentence that begins "although":
The authors wrote:
"Although a significant increase in risk with an increasing number of genital powder applications was found for nonmucinous epithelial ovarian cancer, when non-users were included in the analysis, no trend in cumulative use was evident in analyses restricted to ever users of genital powder."
That's what the authors wrote in their study. Correct?
A. That's what they wrote, yes.
Q. The question of whether a trend in cumulative use was evident in Terry, you've come to an opposite conclusion to the conclusion of the authors of that study with respect to ever-never use?
A. I think they are not talking about ever/never use but dose-response.
Q. I'm talking about a dose-response effect when the analysis is restricted to people who actually used talcum powder.

A. Only users.
Q. Correct.
A. The first part of that sentence says, "although a significant increase in risk with an increasing number of genital powder applications was found for nonmucinous, epithelial ovarian cancer when non-users were included in the analysis."

This is the issue, and I talked about it this morning. When non-users with a comparison -- which is a very valid comparison, there was a statistically significant p-Value. When they were not included, when it was only the users compared among themselves, the p-Value was .17. Those are the two different statistical tests I look at. I also look at the confidence intervals for each of those levels.
Q. Let me focus you on the part I was trying to focus you on. I was trying to focus you on A 139, page 8. The part I was trying to focus you on is the part after the comma. It goes on and says:

"No trend in cumulative use was evident in analyses restricted to ever users of genital powder."

That's what they said. Correct?
A. Yes.
Q. And just for clarification, the issue here is whether or not in calculating a dose-response the

authors of a study include in the calculation of dose-response people who never used talc at all. Right?

A. Yes.

Q. You say for purposes of this matter and for purposes of emphasizing that Terry in your view shows dose-response. You say that the people who never used talc should be included in the calculation. Right?

A. Yes. Although I think it is very appropriate they did it both ways.

Q. And what the author said was that there was no trend if you focused only on people who actually used talc, and then watched what happened if they used more and more over their lifetimes. Fair?

A. Yes. And they also reported when they included non-users.

Q. They reported it both ways. Right?

A. Yes.

Q. You said I think earlier today something to the effect of statisticians favor including those who never used the product, did you say something to that effect?

A. That's my understanding, that unless there is some other reason to exclude non-users, it is appropriate to include them.

Q. What is that understanding based on?
A. That it's appropriate to include non-users when you are looking at a dose-response effect, unless there is some other reason non-users are so different they should be excluded. I liken it to if you are testing a dose for effectiveness in a randomized trial, you would compare to placebo.
Q. If you are testing the effect of a dose, there should a dose. Right? This is a crude example. If someone were testing the effect of drinking beer, you would test the effect of one can of beer versus the effect of 10 cans of beer. You wouldn't necessarily include zero cans of beer?
A. I think you would. We note the test of trends that were -- the two tests of trends we're both referring to are the tests including relative risk. These relative risks were calculated comparing to the non-users.
Q. You said earlier today there was some basis -- strike that.

You said earlier today that statisticians prefer to include people who never used the substance. Tell the Court the basis for that.

Can you cite some periodical or study to that effect.

A. Dr. Sander Greenland, and I don't have the article on the top of my head.
Q. Anything else?
A. That would be the reference I have.
Q. Are you familiar with an epidemiologist named Britton Trabert.
A. He's an epidemiologist?
Q. I believe so, or statistician, one or the other? You don't know the name?
A. I don't.
Q. Let me show you an article and see if you have seen it.

Britton Trabert is a woman. I beg your pardon?

This is a commentary entitled:

"Body powder and ovarian cancer risk, what is the roll of recall bias?"

Authored by Britton Trabert. It is dated 2016. Have you ever read this article before?

A. No, it doesn't look familiar.
Q. Let me direct your attention to the lower right-hand corner of the right-hand column on page -- the first page of the document, which we will mark as McTiernan 521. It says at the bottom of the page, quote:

"In addition, when a pronounced binary association is present use of the never or no category in assessing trend can induce a trend where none exists. The recent OCAS analysis reported no trend with increasing lifetime application when restricted to talc users." And it has a citation to note 18.

Do you see that? And that citation is to the Terry paper.

A. Yes.

Q. Now, you would agree that if the people who did not ever use talc are excluded from the analysis of the dose-response, the conclusion of the Terry paper was that there was no significant dose-response. Right?

A. My conclusion would be that the p-Value is .17 but the relative risks still remain the same. They increase with increasing dose over the four categories.

Q. There was no significant trend if the people who never used talc were excluded from the calculation. Right?

A. The trend was not statistically significant, correct.

Q. Which means that there was no association that you could establish. Correct?

A. It doesn't change the relative risk.
Q. Let's talk about the Penninkilampi study as it relates to -- actually, not that one. Let's do another one.
Let's talk about the Harlow paper.
A. Which one is this?
Q. It is 1992. It is Exhibit A 55.
Do you remember that Harlow 1992 was one of the papers that did use the metric that you say is proper, which is frequency times duration? That's true. Correct?
A. Yes.
Q. Turn to page 8, left-hand column, the first full page. It says:
"As a continuous variable in a multi variate model, no significant dose-response was observed between total genital applications of talc and ovarian cancer risk." Correct?
A. Yes, it states that.
Q. One of the other studies you reviewed is Cook 1997. This is Exhibit A 21?
This is one of the studies you read. Right?
A. Yes.
Q. Your conclusion in your report, if we could call up Exhibit C 7 at page 71 in the chart, that you had

in the back of your report, you listed Cook as a study where there was no cumulative lifetime days, therefore, no dose-response. Is that right, Doctor?
A. I think what that means is no dose-response found and that was the matrix she looked at cumulative lifetime days.
Q. Let's take a look at the study then. Exhibit A 21 in your book is the Cook study. Let me ask you to go there. Please turn to page 6, Table 3. Do you see there is a table where the study includes dose-response?
A. Yes.
Q. And it has information based on cumulative lifetime days of any perineal dusting. Correct?
A. Yes.
Q. It says:
"Any perineal dusting," and it looks at less than 2,000 lifetime days going up to over 10,000 lifetime days, and it lists the results. Correct?
A. Correct.
Q. And so at less than 2,000 lifetime days it is 1.8 risk ratio. Right?
A. Yes.
Q. And then if people use more talc for between 2,000 and 5,000 lifetime days, the risk ratio goes

down. Agreed?
A. Yes.
Q. And the risk ratio goes down for people who use more talc between 5,000 and 10,000 lifetime days. Right?
A. Yes.
Q. If they use more than 10,000, it goes up again. Right?
A. Yes.
Q. That would have been kind of an upside down U if one were to plot it on a graph. Right?
A. Yes.
Q. Did that refresh your memory that the Cook study did not in fact find a dose-response?
A. Yes. And that's what I indicated in that table.
Q. I thought you were saying you were not sure that's what you indicated in the table?
A. If I put the word "no" and "no dose-response," and that the metric is what was in parenthesis.
Q. Let's look at Cramer 19 -- actually, let's look at your table first. It is Exhibit C 7. That's your report of the table, in the back, is page 70, a similar table we used before.
Actually, that's not the right one. We're looking for the entry that says "no lifetime

applications." It is page 70, Table 1, Cramer 1999 entry.

What you wrote here with respect to dose-response for Cramer is:

"Yes, there is dose-response lifetime applications when Fallopian tubes present with an O.R. for less than 3,000 uses of 1.54 and more than 10,000 1.72 as the RR -- excuse me -- between three and 10,000 1.72 and for more than 10,000 1.80."

That's what you cited. Right?

A. Yes. The only correction is "patent" instead of "present."

Q. Now, on this one you did not list a p-Value or say anything about statistical significance, as you did with the Harlow study a few minutes ago on your chart. Correct?

A. Correct, it is not there.

Q. You accurately just stated there is no p-Value listed on your chart because they did not calculate one. Is that right?

A. I don't know. I would have to look at the study.

Q. Will you take my representation that --

A. Yes.

Q. Where in Table 1 can we tell whether the

dose-response data that you chose to include here is for genital talc use as opposed to, for example, non-genital use? Can we tell from reading your chart?

A. Can you tell me which number the paper is?

Q. It is A 23. Exhibit A23 is Cramer 1999. I'll direct your attention in that exhibit to page 5, Table 3. Do you have that in front of you?

A. Yes.

Q. Now, what you reported in your chart that was in the report provided to the Court was that in this area here in Table No. 3 --

MR. WILLIAMS: For the record, I'm focusing on the portion that says "applications censored."

Q. You were referring to the fact that if one used talc less than 3,000 times, the risk ratio was lower than if one used it more than 10,000 times. This portion I'm indicating with the laser. Correct?

A. Yes.

Q. There was another chart for total applications here that listed for people who are using genital talc. It lists less than 3,000 uses a risk and odds ratio of 1.84. Correct?

A. Yes.

Q. An odds ratio for 3,000 to 10,000 uses of 1.43. Correct?

A. Yes.
Q. And an odds ratio of more than 10,000 uses of 1.43. Correct?
A. Yes.
Q. That odds ratio goes down not up with more uses. Correct?
A. Correct.
Q. You could see here this sets forth a p-Value which is 0.472. Correct?
A. Yes.
Q. And that p-Value is more than .05. Right?
A. Yes.
Q. Which means it is not statistically significant. True?
A. Yes.
Q. You chose to use this trend, this set of values, that includes nongenitally exposed people. Right?
A. I believe I did not put a p-Value in the table. I didn't include either one of those p-Values. That's why I was confused why I had nothing there.
Q. What you included in the table, Doctor, was a statement that this Cramer 1999 showed, yes, a dose-response, and then you simply listed the date that appears here under the applications censored group for people including folks who did not use talc

in the genital area; they used it elsewhere. Right?
A. Yes. If I had room in the table, I would have put the relative risk and the confidence intervals and did the p-Value. I would have focused on the genital exposure patients. The issue is, though, I don't know what those RRs referred to, and so I would need to look back at the paper to see that. It looks like they are not giving full data of genitally exposed --
Q. Can we agree, Doctor, if you had focused the Court on the total application PSC date for people who used talc only in the genital area, that you would not have been able to report to the Court that there was a dose-response because there wasn't?
A. But there is in the bottom one, where it is called "pelvic censored," and that is people who had patent Fallopian tubes, and there is some science, the case-control studies, particularly suggesting the risk is greater in people who have patent Fallopian tubes so that the material can move up. If I had room, I could have put both in there.
Q. You can't tell the Court what happens to the statistical significance in the bottom group, the pelvic censored group, when the nongenitally exposed women are excluded; right? You can't do that?
A. They gave the p-Values. They provided it. It's

the relative risk that now I'm saying I can't. But there is a dose-response you can see with confidence intervals that do not include one. The question is which group are those referring to. But my statement is correct. There is a dose-response in that group.

Q. Right here in the portion that relates to people who actually used talc in the perineal area, there is data under "total applications" that does not have a statistically significant result. Correct?

A. If you look at patent, which I've stated on the table, then you see that.

Q. Just a yes or no if you can give it. There is data on this table for total applications that includes people who use talc in the perineal area, and that does not show dose-response. True or not true?

A. If I reported on that table, I would say that, but I reported on the other table.

Q. And the answer is yes?

A. The question again was?

Q. I'll move on.

Let's go to a study called Mills 2004. This is a retrospective case-control study by Mills. You reviewed this data. Correct?

A. Yes.

Q. Please take a look at page 4, Table II. This is

Exhibit A 94. This includes data on dose-response. Correct?

A. Yes.

Q. And there is a portion that talks about cumulative use frequency times duration. Right?

A. Yes.

Q. It include never users?

A. Yes.

Q. It include four different quartiles. Correct?

A. Yes.

Q. And it lists in the right-hand column odds ratios for each of those quartiles. Correct?

A. Yes.

Q. The first quartile, meaning the lowest exposure calculated using the metric you say is the best one frequency times duration, it reports 1.03 as the point estimate. Correct?

A. Yes.

Q. And that value is not statistically significant. Correct?

A. Yes.

Q. The second quartile people who use more talc than people in the first quartile, the result is 1.81 statistically significant. Right?

A. Correct.

Q. The third quartile goes down. That's for people who used more talc than those in the first two quartiles. True?
A. Correct.
Q. It goes down to 1.74. Right?
A. Correct.
Q. And for people who are have the highest exposure which is who reported the most use calculated by frequency times duration, the odds ratio is 1.06. Not statistically significant. Correct?
A. Correct.
Q. This study does not show a dose-response. Correct?
A. I agree. That's what I indicated in my table.
Q. Right. In your table, if you add them all up -- I'm not going to ask you to do it now. It will take too long -- there are a number of studies that analyze frequency times duration that show no dose-response and some that purport to show a dose-response. Is that right?
A. I haven't added it recently. I did it for my report, but I don't know the exact numbers.
Q. I'm not asking you to add right now. There are some that show a dose-response and some that do not.
A. Correct.

Q. We have talked about the Terry study and your conclusions there and your calculations. Right?
A. Yes.
Q. That is one of the ones you said showed dose-response. True?
A. Yes.
Q. We talked about Cramer 1999. That's another you said showed a positive dose-response. True?
A. Yes.
Q. Let's move on.

The most thorough case-control studies in your opinion were those that differentiated among different areas of exposure to talc.

A. Are you citing something in my report?
Q. I am.
A. I want to see what it refers to.
Q. By areas of exposure, I mean perineal use. One area of exposure is the use of talcum powder products on the diaphragm. Correct?
A. Correct.
Q. Please turn to the Cramer 2016 study we marked earlier. It is A 25. Do you have that in front of you?
A. Yes.
Q. Table 1 is entitled type, "Timing and Duration

of Genital Talc Use." Right?
A. Yes.
Q. It lists potential exposure in women with no personal use. Right?
A. Yes.
Q. And it pulls out diaphragm only use. Correct?
A. Correct.
Q. And we're talking about diaphragms that have some sort of talc on them. Right?
A. Is that how they define it?
Q. Let's look at what the data shows.
A. I want to see how they asked -- I want to check how they are asking about the diaphragm use.
I see, yes, they have that.
Q. That's the reason why it would be relevant because if a woman had talc on her diaphragm and inserts the diaphragm, it is closer to the ovaries than if a woman dusts herself outside, say, in her panties. Correct?
A. It did not ask if they rinsed it off prior to applying spermicidal jelly, so we don't know about talc from that question.
Q. What the results indicated were that people who used the diaphragm, and that was their exposure to talc, the odds ratio was 0.73 with a statistically

insignificant confidence interval of 0.57 to 0.93. Correct?
A. No. The traditional interpretation of a confidence interval is where it includes 1. This does not.
Q. It does not include 1?
A. So that would suggest statistical significance around that odds ratio.
Q. I beg your pardon. Because the odds ratio is below 1, and because the confidence interval does not hit 1.0, this is statistically significant?
A. Yes.
Q. So the result is a statistically significant finding of a protective effect for the use of a diaphragm with talc on it. Correct?
A. Yes. With the caveat we don't know if the woman rinsed the diaphragm before putting spermicidal jelly and before inserting. So we don't know about the amount of real exposure.
Q. Are we assuming every woman in the study --
A. Some women would have been instructed to do it that and some not.
Q. You know that the study did not do that?
A. I don't know that they asked about whether they rinsed it or not.

Q. You don't know one way or the other they did?
A. Right.
Q. But we do know there is a statistically significant finding of a protective effect, meaning if the epidemiological evidence is credited, it would mean if the women used the diaphragm with talc on it, she would have a lower chance of getting ovarian cancer. Correct?
A. If there was talc on it. That's what we don't know.
Q. Let me have you look at the Berge study, the 2018 meta-analysis. This is one of the studies you said was excellent. Right?
A. Which number is this?
Q. A 11. I'll direct you to Table II on page 7. Do you have that there?
A. Yes.
Q. This study, one of the ones that you say was excellent in terms of its methodology, lists with one of its findings for the use of a diaphragm a statistically significant protective effect odds ratio of 0.75 with a confidence interval that does not cross 1, 0.73 on the low end to 0.88 on the high end. Correct?
A. Yes.

Q. Please turn to the Penninkilampi study. That's Exhibit A 109. Please look at page 5.

Page 5 has a table, Table 1, that like the other studies we just looked at, references diaphragm use. Correct?

A. Yes.

Q. And it references the method of talc use suggesting talc was on the diaphragm. Right?

A. Yes.

Q. This one is not statistically significant because it crosses 1.0. Correct?

A. Yes.

Q. But the finding was 0.84 as the odds ratio. Correct?

A. Yes.

Q. So if it had been statistically significant, like the other two studies we just looked at, it would have had a protective effect. Correct?

A. Yes.

Q. Earlier today you testified on direct examination that an odds ratio of 1.4 is -- strike that.

You testified an odds ratio of 1.4 has in the past sufficed for purposes of findings there is a causal connection between a substance and some

disease. Correct?
A. I don't recall talking about causality. I recall talking about some additional risk factors in the low range.
Q. You talked about HRT, did you not?
A. Yes.
Q. Let's take a look at your report and what it said about HRT. That's hormone replacement therapy, for the record. That's Exhibit C 7, page 26. Is that the portion of your report?
Doctor, that references HRT?
A. Yes.
Q. There is a sentence that starts at the bottom of 26 and carries over; and at the end of that sentence it has a citation to number 55, reference number 55. Correct?
A. Yes.
Q. If you go to page 80 of your report -- let's look at that reference. Do you have that in front of you?
A. Yes.
Q. That reference 55 is to a study written by Rossouw. It is from 2002. Correct?
A. Yes.
Q. This was a study you cited talking about the

principal results from the Women's Health Initiative Randomized Control trial. Right?
A. Yes.
Q. So with respect to HRT, a randomized control trial had been conducted that showed the association. Right?
A. Yes.
Q. There hasn't been a randomized control trial, nor could there be, in your view, for talcum powder?
A. That's correct.
Q. It goes on on the next sentence at the top of page 27. The sentence says:
"A meta-analysis of clinical trials and observational studies in 2018 found that use of this therapy increased risk of breast cancer by 59 percent."
Did I read that right?
A. Yes.
Q. And it cites item 56. Correct?
A. Yes.
Q. Let's turn to page 80 and see what item 56 is. That was a study by Kim dated 2018. Correct?
A. Yes.
Q. It says:
"Menopausal Hormone Therapy and the Risk of

Breast Cancer By histological Type and Race: A Meta-Analysis of Randomized Controlled Trials and Cohort Studies."

Did I read that right?

A. Yes.

Q. So here there were not only randomized trials but there were cohort, forward-looking cohort studies with respect to HRT. Right?

A. Yes.

Q. That's very different than the situation before Her Honor, is it not?

A. In terms of?

Q. In terms of whether or not there have been randomized control trials. Right?

A. Correct.

Q. What you are focusing on for purposes of your testimony is case-control studies and cohort studies. Correct?

A. Yes.

Q. But the cohort studies for our purposes are all studies that find no statistically significant association between the use of talc and ovarian cancer. True?

A. Correct.

Q. Let me ask you some questions on confounding.

For the talc studies that presented both adjusted and unadjusted risk ratios, your opinion is that those studies found little effect of confounding variables. True?

A. Yes. For the studies that showed both the unadjusted odds ratios and the adjusted odds ratios, nine out of 10 of them had very similar results.

Q. You believe that all, all except for one of the talc studies that you reviewed performed adjustments for several potential confounding variables?

A. Yes.

Q. And you agreed this morning or you stated this morning on direct examination with plaintiffs' counsel, you said that your systematic analysis examined whether or not a study adjusted for confounding. Do you remember saying that?

A. Yes.

Q. But the truth is, Doctor, that you did not actually look at the specific confounding or confounders for each of those studies. Right?

A. I did look at the tables in which they indicated confounders. They were different in each study. I assumed that they reported the ones that they adjusted for.

Q. You did not look at the specific confounders for

each of the studies?
A. I did look at confounders. I read through the tables and list of variables they listed.
Q. Please take a look at your deposition, page 175, line 25 to 176, line 16:
"QUESTION: Without reviewing the study, are you able to tell us, as you sit here, how many of the case-control studies you read and reviewed and are relying on in this case do not adjust for body mass index?
"ANSWER: No, I did not count that.
"QUESTION: Why not?
"ANSWER: I was tasked to look at the overall association. I did not look at specific confounders for each of the studies."
That was your testimony. Right?
A. I see what you mean. For my expert report, I did not go through and mark for which studies adjusted for BMI and which did not, but I did look at the studies to see what variables they adjusted for as I reviewed them.
Q. My question was whether I read correctly your testimony. Did I do that?
A. To me it looks like the testimony you were asking then was about body mass index, BMI.

Q. Did I read it correctly? Was that your testimony?
A. I'm not sure which section you are talking about.
THE COURT: He's not asking you to comment upon. He wants to know what he read to you, was that accurate? What he read, does that appear in the transcript you testified to?
THE WITNESS: Yes.
BY MR. WILLIAMS:
Q. One of the items that you placed on your bases for finding a causal association between talc use and ovarian cancer, you referenced IARC. Right?
A. Yes.
Q. And you are familiar with that agency because you've done work for them. Right?
A. Yes.
Q. You know that IARC has five different categories into which it places substances. Right?
A. Yes.
Q. Group 1 is substances that IARC believes are carcinogenic to humans. Right?
A. Yes.
Q. Group 2 A is for substances IARC believes are -- probably carcinogenic. Right?

A. Yes.
Q. Group 2 B is for substances that IARC believes are possibly carcinogenic. Right?
A. Yes.
Q. Group 3 is for substances that are not classifiable. Right?
A. Yes.
Q. And Group 4, finally, is for substances IARC believes are probably not carcinogenic. Right?
A. Yes.
Q. You know, there is only one substance that has ever been placed in Category IV?
A. I knew it was very small.
Q. In 2006 IARC listed perineal use in the 2-B category. Correct?
A. Yes.
Q. That's 2-B, possible carcinogenic. Right?
A. Yes.
Q. Please take a look at the IARC monograph. It is Exhibit A 72 K. It is a really long document. Sorry about the length. I would like you to look at page 46 of the 2010 IARC monograph on talc.

Do you have that in front of you?

Using the numbers at the bottom of the page, page 46. It's also on the board. See there is a

reference to Group 2 B?
A. Yes.
Q. And this category is used for agents for which there is "limited evidence of carcinogenicity in humans and less than sufficient evidence of carcinogenicity in experimental animals."
Do you see that?
A. Yes.
Q. Please turn now to page 42, a few lines earlier. The term "limited evidence of carcinogenicity" is a defined term in the monograph. Correct?
A. Yes.
Q. There is a definition at the bottom of this page, page 52, for "limited evidence of carcinogenicity." Right?
A. Yes.
Q. The definition is:
"A positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered by the working group to be credible, but chance, bias, or confounding could not be ruled out with reasonable confidence."
Right?
A. That's what it says, yes.
Q. So IARC was saying it could not rule out chance

or luck with respect to talcum powder use, perineal use, and ovarian cancer. Correct?
A. At the time when they reviewed the data which I believe was about 2008. So 10 years ago.
Q. This is the IARC monograph from 2010, but they looked at the data before that. Right?
A. Yes.
Q. IARC was also saying that it could not rule out bias. Right?
A. Yes.
Q. You understand that to mean recall bias. Correct?
A. It could be any bias.
Q. And IARC was also saying it could not rule out confounding factors. Correct?
A. Correct.
Q. Now, IARC has never moved perineal talc up to a higher classification than Group 2 B. Right?
A. But they are going to reconsider it. They classified it as high priority for review again.
Q. Do you have any knowledge one way or the other how many items are listed on that elevated interest list?
A. It is a minimal number. I believe we added that to the list.

Q. Do you know how many?
A. I believe we added that to the list of items.
Q. Let me ask you this: As of today at this point in time when the Court is assessing whether or not sufficient evidence exists to say that talc causes ovarian cancer, as you have opined, IARC still lists perineal talc use as a Group 2 B substance. Correct?
A. They have not reviewed it again yet.
Q. The answer is yes?
A. Yes.
Q. When you say IARC would reach a different conclusion now -- strike that.

Do you think IARC would reach a different conclusion now? That was the suggestion you are making by saying they may prioritize a review. Are you saying their conclusion would be different?
A. I can't speak for their working group. I don't know who would be on it. I don't know what they would decide, but I do know the evidence looks quite different now than it looked 10 years ago.
Q. So if you were to suggest to the Court the conclusion would be different, you would be speculating. Right?
A. I said I don't know who is going to be on the committee. I don't know what they would state. I do

know the evidence has changed, but I can't say how they would vote.

Q. My question is different. If you were to say that IARC would change its opinion today, you would be speculating?

A. Yes.

Q. In order for IARC to move a substance from Group 2 B possible to a higher group, IARC would have to rule out chance, bias, and confounding factors, all three. Correct?

A. I haven't read the exact criteria for the next level up.

Q. You mentioned Health Canada. Let me ask you a few questions about that.

You identified 127 documents or other materials as references in your litigation report. Correct?

A. Yes.

Q. Those materials that you relied on to form the basis of your opinions in this case, right, those are all of the materials. Correct?

A. Yes.

Q. None of the documents on your reliance list was published by the Food and Drug Administration. Correct?

A. I don't recall if I included the letter from them. I don't recall. I would have to look through.
Q. None of the documents -- I'll get to that in a second. None of the documents on your reliance list was published by the National Cancer Institute. Correct?
A. The National Cancer Institute itself, not a grant that was funded through the National Cancer Institute.
Q. Let's take both. How about by NCI itself?
A. I don't recall including anything that was from NCI.
Q. And branches of NCI --
A. Several of the studies I mentioned were funded by NCI.
Q. Funded by NCI is one thing, put out by the organization itself is another. Right?
A. Yes.
Q. Your litigation report identified another 113 documents as materials considered, right, in addition to the references?
A. I don't know the exact number, but I'll believe you, yes.
Q. A few of those documents were led, sent to the FDA. Do you remember that?

A. I don't recall.
Q. Take a look at Exhibit C 7, your report, page 86.
A. Is it in Volume 1 or Volume 2?
Q. It is in Volume 2. It is your report. It is C-7.
A. Okay.
Q. Take a look at page 86. All I want to focus you on are items 68 to 70. See those?
A. Yes.
Q. Those are all letters from the Cancer Prevention Coalition to the FDA; are they not?
A. I see two of those, yes.
Q. None of those 113 additional materials and data considered were authored by the FDA. Right?
A. I don't see it here.
Q. None of those documents were published by the NCI. Right?
A. None of these -- the numbers you gave me, none say "NCI," no.
Q. If you would take a look at Exhibit A 89, I believe, this was not a document you actually relied upon for your opinions in the case. It is one you heard about that talked about migration. Do you recall that?

A. Yes.
Q. This one is the letter dated April 1, 2014, and I'll direct your attention to the first paragraph on the third page. This is a document that was responsive to the three or four letters that we just looked at on your reference list that were to the FDA. You recall those letters, right?
MS. PARFITT: I object. It is on her reliance list, the FDA 2014 letter. Counsel is suggesting she didn't rely on it. That was my understanding of your question.
MR. WILLIAMS: That was my understanding. I thought the witness testified it was not on the reliance list. If it is, I'm mistaken. But that doesn't matter for purposes of my question.
THE COURT: That's fine.
Q. Doctor, I'll ask you this: Whether or not it is on your reliance list, what the letter said in response to those citizens' petitions was paragraph 3:
"After careful review and consideration of the information submitted in your petitions, the comments received in response to the petitions, and review of the additional scientific information, this letter is to advise you that FDA is denying your petitions. FDA did not find that the data submitted presented

conclusive evidence of a causal association between talc use in the perineal area and ovarian cancer."

Did I read that correctly?

A. Yes.

Q. So you focused the Court on the Health Canada draft study. Correct?

A. Yes.

Q. You did not point the Court to your review reflecting that government agencies in the United States like the FDA have found that the evidence is insufficient to find a causal association. Right?

A. Right. I don't know if the FDA has done a systematic review like Health Canada does. I have not seen a publication of systematic review and causal analysis from the FDA. This is what I've seen, this letter.

Q. You don't know one way or the other whether the careful review that is referred to in Exhibit A 89 was a systematic review by your definition?

A. They don't reference a systematic review and they don't reference a publication.

Q. It is accurate to say that your conclusion here is inconsistent with the conclusions set forth by the FDA in its letter in response to the petition?

A. That's correct.

Q. Just a couple more things.

First I wanted to make sure that --

MR. WILLIAMS: Your Honor and counsel, this is the McTiernan report, Exhibit C 7, page 13, description of a confidence interval, forward.

Q. I put up a board and I wanted to ask you, Doctor, it says:

"If a confidence interval includes the number 1.0, then we say the association between the exposure and the disease could be null."

Did I read that right?

A. Yes.

Q. That is your writing in your report. Correct?

A. Yes.

Q. Now, if a confidence interval in a study were to be exactly 1.0, that would be no association. Correct?

A. I don't know what the relative risk is that you are referring to.

Q. I misspoke.

If the relative risk were reported as 1.0, that would mean no association. Correct?

A. Yes.

Q. That is to say, if the point estimate were 1.0, that would be no association. True?

A. Correct.
Q. Okay. If the confidence interval, the range, includes 1.0, that is, it goes above and below 1.0, you cannot say that there is an association. Right?
A. What we can say is that the association between exposure and disease could be null. So it could be. That's exactly what I said here, that it could be null.
Q. Let me ask you some questions about your -- you mentioned you spoke to Congress, and I just have a couple of questions about that.
You indicated you were asked to speak to Congress. Who asked you?
A. I believe his name was Mr. Cunningham. He was the Chief of Staff for that subcommittee.
Q. Do you know how that particular subcommittee got your name?
A. I don't know.
Q. Your litigation report in this matter is dated November 16th of last year. Correct?
A. If that's what's here, I believe it.
Q. A few months later after that you appeared before the subcommittee of Congress. That was on March 12th of this year. Right?
A. Yes.

Q. You read aloud from a prepared statement that day. Correct?
A. Yes.
Q. And you were asked to give that testimony -- I think you said this when you spoke that day -- because you had conducted a thorough and systematic review of the science linking use of talcum powder products and the risk of ovarian cancer. Right?
A. That's correct.
Q. Now, do you know whether or not anybody from Johnson & Johnson was asked to attend that hearing?
A. I don't know.
MS. PARFITT: Objection, your Honor. I can't imagine how Dr. McTiernan would know if anyone from Johnson & Johnson --
THE COURT: I think she already answered it. She said "I don't know."
Q. When you appeared that day you were accompanied by several of the plaintiffs' lawyers, is that right, who are in the room today?
A. There were several people there. The main person accompanying me was the Vice President for Government Affairs at my institution, Fred Hutchinson.
Q. And Ms. Parfitt was there and Ms. O'Dell was there?

A. Yes. And several other people in the room.
Q. Did you know beforehand plaintiffs' counsel would be attending?
A. Yes.
Q. Do you know whether plaintiffs' counsel played any role in your being invited to testify?
A. I don't know.
Q. You don't know one way or at the other?
A. I don't know.
Q. Did you meet with plaintiffs' counsel in advance of hearing? I don't want to know what you said to them or them to you, but did you meet with them prior to the hearing?
A. Yes.
Q. Did you travel to the hearing with them?
A. No -- travel to the meeting with them?
Q. Yes. Did you go over to Congress with them that day?
A. Yes.
Q. Now, did you share a copy of your written statement to the subcommittee with plaintiffs' counsel before you testified?
A. I did, and also to my Vice President of Government Affairs.
MS. PARFITT: Your Honor, I object at this

point in time. I understand how the substance of Dr. McTiernan's opinions are relevant, but I think we have gone a bit afield as to how she got there. It is clear I was there. Ms. O'Dell was there. I'm just not sure where we are going.

MR. WILLIAMS: Counsel raised the issue. I did not.

MS. PARFITT: I raised the issue of her appearance before Congress.

THE COURT: I understand. I'll permit a few questions.

I don't know if you have anything else. I know where you are going with it.

MR. WILLIAMS: There is actually a little bit more.

THE COURT: Let me hear it.

BY MR. WILLIAMS:

Q. You told the subcommittee your opinion that perineal talc use is associated with a 22 to 31 percent increased risk. Right?

A. Yes.

Q. You did not talk about cohort studies?

A. I didn't talk about specific studies. I talked about totality of evidence.

Q. You did not talk about the cohort studies saying

there is not an association. True?
A. No, I did not.
Q. Now, in the written materials that you provided, you mentioned that you had been hired by plaintiffs in litigation.
THE COURT: You are referring to written materials she provided to Congress.
MR. WILLIAMS: Yes.
A. Yes, I disclosed, yes.
Q. You disclosed there that you had been hired by plaintiffs in litigation. Right?
A. Yes.
Q. But in your oral presentation -- which was televised; am I right?
A. Yes.
Q. In your oral presentation, you did not say that you were hired by plaintiffs' lawyers in litigation, did you?
A. I don't recall.
Q. In your oral presentation you said that you were there on behalf of consumers. Right?
A. I don't have the document right with me.
Q. Let's see if we could bring it up.
A. Can you tell me what number it is so I could look at the whole thing?

Q. It is McTiernan 510 in your book. That would be in book No. 2.

My only point is that when you were speaking as opposed to the writing, when you were talking on television, you said as part of this review, I prepared an expert report on behalf of consumers for an ongoing multi-district litigation. Right?

A. Oh, so I did disclose. Okay.

Q. The word you used was "consumers," not that you were hired by plaintiffs' counsel on behalf of plaintiffs in litigation?

A. I didn't use that word, no.

Q. You did not indicate in any way that you were there as an expert who was being paid in litigation on behalf of specific plaintiffs, did you?

A. I didn't use the word "paid," no.

Q. Nor did you use the word "plaintiffs." Right?

A. I didn't use the word "plaintiffs," no.

Q. And you changed the wording that was contained in your written submission that you used the word "plaintiffs." Right?

A. I'm sorry. I can't remember what I said. I just know that I disclosed there. I thought I disclosed here. I don't know what that wording was to compare.

MR. WILLIAMS: Thank you, your Honor. No further questions.

MS. PARFITT: Do you want to break or go forward?

THE COURT: I'm good if you are.

Let's take a break.

THE DEPUTY CLERK: All rise.

(Recess.)

(Continued on the next page.)

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THE DEPUTY CLERK: All rise.

THE COURT: Thank you.

ANNE MC TIERNAN, resumed.

REDIRECT EXAMINATION

BY MS. PARFITT:

Q. Good afternoon, Dr. McTiernan. I'm going to try to move as quickly as I can.

MS. PARFITT: And I appreciate the Court's indulgence.

Q. Dr. McTiernan,, you were asked about your Congressional presentation?

A. Yes.

Q. And you indicated that I was there and Ms. O'Dell was there. Correct?

A. Yes.

Q. Were there victims there, too?

A. Yes, there were.

MR. WILLIAMS: Objection. Not appropriate.

THE COURT: They were going to object to the word "victims."

Q. Were there "consumers" there?

A. Yes.

Q. Did the consumers also make statements?

A. Yes. There was one that did.
Q. Do you recall what the statement was?
A. I don't recall his exact statement. He was the son of a woman with ovarian cancer who passed away from the disease.
Q. Are you aware whether or not any J&J employees were there?
A. I don't know.
Q. Now, were you paid by the plaintiffs' counsel here to show up for Congress?
A. No.
Q. You came on your own volition?
A. I came as an independent scientist.
Q. Now, throughout the course of the day -- if we could throw up the forest plot.

Now, counsel asked you many, many questions about your opinions on consistency. Do you recall those questions by Mr. Williams?
A. Yes.
Q. Specifically, he talked about the consistency and the role of statistical significance among epidemiological studies. Do you recall that?
A. Yes.
Q. Do you recall Mr. Williams made a distinction between not what the relative risk was but p-Value or

whether something was statistically significant or not statistically significant for purposes of consistency? Do you recall that examination?

A. Yes.

Q. What I would like to do -- do you know who Kenneth Rothman is?

A. Yes.

Q. Who is Dr. Rothman?

A. He's an epidemiologist who specializes in the methodology of epidemiology and the applications of statistics. I took a course from him in 1977. So I learned his methods early on, and in my Ph.D. program my mentor was a colleague of his. They both trained at Harvard. So I continued to use similar methods after that training.

Q. Are you aware Dr. Rothman, along with Sander Greenland and Timothy Lash published A Modern Epidemiology book?

A. Yes.

Q. Are you familiar with that book?

A. Yes.

Q. What I would like to do is pull up Chapter 2, page 27, of the Modern Epidemiology, Third Edition, by Doctor Rothman, et al.. At the top of the page it says: Chapter 2, "Causation and Causal Inference."

Do you see that?
A. Yes.
Q. Then there is a section on "Consistency." Do you see that?
A. Yes.
Q. Why don't you go down to the second full paragraph, and let me ask you a question.
Dr. Rothman states:
"One mistake in implementing the consistency criterion is so common that it deserves special mention. It is sometimes claimed that a literature or set of results is inconsistent simply because some results are statistically significant and some are not. This sort of evaluation is completely fallacious even if one accepts the use of significance testing methods."
Did I read that correctly?
A. Yes.
Q. Do you agree with Dr. Rothman?
A. Yes.
Q. Is that opinion consistent with not only that which you shared with the Court today but with Health Canada, the regulatory body for Canada and Congress?
A. Yes.
Q. Dr. McTiernan, you were asked about IARC's

classification of talc back in 2006 when the working group considered it. Do you recall those questions?
A. Yes.
Q. And you understand, Dr. McTiernan, that IARC's monograph that was published in 2010 was based upon what?
A. It was based upon talc without fibrous talc, and it was with the assumption it did not contain asbestos, and it was based on studies up until a couple of years or a year prior to when they did their deliberations.
Q. So the evaluation of IARC back in 2006 was literature up until 2006, and that would include literature on biological plausibility. Correct?
A. Yes.
Q. That would include literature on anything with regard to pathology. Right?
A. Yes.
Q. That would include literature with regard to mechanistic studies?
A. Yes.
Q. And that would include the epidemiological literature. Correct?
A. Yes.
Q. Have you had an opportunity to review IARC's

2012 monograph?
A. Yes, I have.
Q. And how is talc with asbestos classified in IARC 2012?
A. It is classified as Class 1, the highest level.
Q. The highest level of what?
A. Carcinogen.
Q. Now, you were asked about biological plausibility by Mr. Williams. Does one need a direct and precise evidence of mechanism in order for there to be biological plausibility?
A. No.
Q. Dr. McTiernan, is asbestos an inflammatory agent?
A. Asbestos can cause inflammation, yes.
Q. Can fibrous talc cause inflammation?
A. Yes.
Q. Do both asbestos fibrous talc and heavy metals provide further evidence of a biological plausible explanation that talcum powder products can cause ovarian cancer?
A. Yes.
Q. You were asked several questions about the Penninkilampi study and the Berge study. Do you recall those?

A. Yes.
Q. And, specifically, with regard to the issue of dose-response -- you were asked by counsel about some individual source case-control studies. Do you recall that?
A. Yes.
Q. What I would like to talk to you about are the meta-analyses that were done 2018, just last year.
If I understand your testimony correctly, the meta-analysis that were done in 2018 by Berge and by Penninkilampi included the aggregate epidemiological literature on talcum powder products and ovarian cancer. Is that correct?
A. That's correct.
Q. So those authors looked back. They didn't take a snapshot in 2006 or a snapshot in 2003, but they did a look-back at the epidemiological literature. Is that correct?
A. That's correct, and included all of the studies that had been done before that time.
Q. That included Dr. Cramer's study back in 1982. Is that correct?
A. Yes.
Q. Let's talk for a minute on Penninkilampi. A couple of questions. You were asked specifically with

regard to the Berge study whether or not there was heterogeneity in the case-control study. Do you recall that question?

A. Yes.

MS. PARFITT: Cory, would you please bring up Penninkilampi and, specifically, if you would kindly go to page 46.

And if you would highlight that first full paragraph.

Q. Let me read:

"This meta-analysis had several strengths. None of the analyses in this review had statistically significant heterogeneity except for the non-perineal application, which indicates consistency in the direction and magnitude of the effect size between individual studies and strengthening the reliability of the pooled effect sizes."

Did I read that correctly?

A. Yes.

Q. What does that -- what does "heterogeneity" mean? What are they telling us about the consistency of the case-control and cohort studies, because Penninkilampi was case-control and cohort? Correct?

A. Yes.

Q. What are they telling us?

A. From meta-analysis it is common to test whether there is heterogeneity; do the individual studies vary greatly from the overall summary relative risk?

First of all, the meta-analyses should do this. It is good methodology. And when they say there is no significant heterogeneity that suggests similar to the points we see on the forest plot, when they test that statistically, things are looking like they track quite well across the studies. The average relative risk reflects what the studies in aggregate are showing.

Q. So when we were looking at the case-control cohort studies a little bit earlier, we were looking at this forest plot of case-control and cohort studies and talking about heterogeneity, what is it about that forest plot of case-control and cohort studies in 1982 all the way up to 2018? How does that speak to the lack of heterogeneity?

A. This is my forest plot, and this shows the studies except for two are to the right. So they are all trending in the positive direction. Looking at the bottom line what these numbers represent.

Q. Are you talking about these?

A. Yes, it goes from negative .2 up to 4. At the largest relative risk is 4. So you really see what

this is referring to. Most of the relative risks are in the same range as what the overall relative risk that the two meta-analyses have found. So it is a very consistent finding, very consistent set of studies.

Q. Similarly, you were asked about dose-response. Do you remember that series of questions?

A. Yes.

Q. What did the Penninkilampi authors find with regard to dose-response?

Let's put it up. Let's go to page 45.

MS. PARFITT: For the record, it is Exhibit 62.

THE COURT: Thank you.

Q. Go ahead.

A. So they looked both at long-term use and at number of total lifetime applications.

MS. PARFITT: Cory, if you could highlight down that last paragraph on the right.

Q. Does that help?

A. They found a greater risk of ovarian cancer with more than 3600 lifetime applications compared to those with fewer lifetime applications.

I would like to point out again the data. That's what I like to look at, the data table.

Q. That's Table II.
A. In the middle here, where it says "length of use," that whole four lines there, that shows what the numbers "O" were. So less than 3600, the relative risk was 1.32. Over that amount was 1.52. The confidence intervals did not include 1.
They also look at long-term use. That was 10 years or more, and they found a relative risk of 1.29. Also confidence intervals did not include 1.
Q. Dr. McTiernan, you were asked about the FDA letter of 2014. Correct?
A. Yes.
Q. You were asked whether the FDA had made a causal analysis. Is that correct?
A. Yes.
Q. I believe your response was you did not see they had done a systematic review. Correct?
A. Correct.
Q. Did Health Canada do a systematic review, and Bradford Hill analysis?
A. Yes, they did.
Q. Let's see what they had to say about causality.
MS. PARFITT: Cory, if you could pull up the Health Canada assessment. Specifically, if you could go to -- okay.

Q. Focusing your attention at the next-to-the-last paragraph, it states:

"The meta-analysis of the available human studies in the peer review literature indicate a consistent and statistically significant positive association between perineal exposure to talc and ovarian cancer. Further available data are indicative of a causal effect."

Did I read that correctly?

A. Yes.

Q. Do you agree with the opinion of Health Canada with regard to the fact that based upon the meta-analysis, the peer-reviewed literature that not only is there a statistically significant positive association between perineal exposure and talc, but the available data are indicative of a causal effect?

A. Yes.

Q. Is that consistent with the opinions you have shared with this Court today?

A. Yes, it is.

Q. Let's go back to Penninkilampi. Page 47. Under "Conclusions."

Penninkilampi is a 2018 meta-analysis. Correct?

A. Yes.

Q. Under "Conclusion":

"The results of this review indicate that perineal talc is associated with a 24 percent to 39 percent increased risk of ovarian cancer. While the results of case control studies are prone to recall bias especially with intense media attention following commencement of litigation in 2014, the confirmation of an association in cohort studies between perineal talc use and serious invasive ovarian cancer is suggestive of a causal association."

Did I read that correctly?

A. Yes.

Q. Do you agree with the authors of Penninkilampi?

A. I do.

Q. Are you aware of any more recent meta-analysis since the Berge, Penninkilampi and the Health Canada report?

A. Yes. Another meta-analysis was referred to and made available with Health Canada by Taher, et al.

Q. Are the conclusions of Health Canada, the Penninkilampi meta-analysis and the Berge meta-analysis all concluding that there is a causal relationship?

A. Yes.

Q. I should not have included Berge in that. You

talk about that?
A. The data are remarkably consistent among those three meta-analyses.
Q. When you looked at the Berge, regardless of what the narrative is, what is it that you look at?
A. I look at the data.
Q. And what does the data tell you in the Berge study?
A. The data tells me that there is a statistically significant increased risk of ovarian cancer in women that used genital talcum powder products compared to non-users.
Q. What does the data tell you in the Berge study with regard to any increased risk in dose-response?
A. The Berge also looked at dose-response in models and they found statistically significant association with increased duration and increased frequency of use.
Q. Berge was a 2018 meta-analysis?
A. Correct.
Q. You were asked at the start of Mr. Williams' discussion with you about pleurodesis. Do you recall that?
A. Yes.
Q. Dr. McTiernan, are you aware of any

peer-reviewed literature that indicates whether pleurodesis is associated with adverse effects and it is not advised in patients without malignant pleural effusions?

A. Yes. Some clinical groups are recommending that talc not be used for this instance. There was one study that found that small size talc powders were associated with adverse events and --

MR. WILLIAMS: I hate to interrupt. I believe this is a new opinion.

MS. PARFITT: Your Honor, she was cross-examined by Mr. Williams on the issue of pleurodesis and its health effects. Pleurodesis was a positive thing. It is only fair I be permitted to ask Dr. McTiernan if there are any studies with regard to the adverse effects.

MR. WILLIAMS: Counsel raised pleurodesis on direct examination. This is new. The only reason I raised it is they raised it.

MS. PARFITT: She's commenting on a study where she's indicating the adverse effects.

THE COURT: I have a general answer now and no more beyond that.

MS. PARFITT: Thank you.

BY MS. PARFITT:

Q. Now, if I can direct your attention to the Bradford Hill statement, and, again, that is Exhibit 1.

Let me did direct your attention to page 11, interval, under "tests of significance."

Dr. McTiernan, referring to the Bradford Hill statement, specifically what Bradford Hill had to say about tests of significance, it read:

"No formal activities of significance can answer those questions. Such tests can and should remind us of the effects that the play of chance can create, and they will instruct us in the likely magnitude of those effects. Beyond that, they contribute nothing to the proof of our hypothesis."

Did I read that correctly?

A. Yes.

Q. Do you agree with Sir Bradford Hill?

A. I do.

Q. I may have misunderstood Mr. Williams' question. I hope I'm not redundant on this. Do you recall you were questioned with regard to your definition of a pooled study? Do you recall that?

A. Yes.

Q. Let me direct your attention to the Terry study itself.

MS. PARFITT: And if you would, Cory, go to page 815.

Q. Dr. McTiernan,, how did you characterize or what kind of study design did you characterize the Terry study?

A. It is a pooled analysis.

Q. What did the authors of the study -- how did they characterize their study?

A. As a pooled analysis.

Q. They say this pooled analysis of eight case control studies, including 9,859 controls and 8,525 ovarian cancer cases?

A. Yes.

Q. Is that a large study?

A. Very large, especially for ovarian cancer which is a rare cancer.

Q. What meaningful information can that provide in a study of that size?

A. You would have much better ability to determine relative risk, to determine the statistical significance, to look at dose-response, to look at subgroups.

Q. The questionnaire for the WHI, the study you were project director for, how did they define talcum powder? Was it all powders? Was it talcum? How it

was it defined?
A. The question was about powder applied to the private area, and they gave examples of talc, deodorizing powder, or baby powder.
Q. Similarly, in the Nurses', the health study, what was the definition of the powder?
A. The question was about powder applied to the perineal area, also with an explanation of talc, baby powder, and deodorizing powder.
Q. The Sister Study, the third cohort study, how was that question defined?
A. Specifically about talc.
Q. So two out of the three cohort studies asked generally about powder, talc, cornstarch, deodorizing powder. Is that correct?
A. That's correct.
Q. What impact would that question have on the relative risk?
A. It would reduce it, attenuate it, toward the null, towards 1, because you have less complete information on use of talc. The women who used other powders would be mixed in with talc users.
Q. So this error of misclassification would occur?
A. Yes.
Q. That would attenuate it further towards the

null?
A. That's right.
Q. In other words, the study results would be lower?
A. Would be lower than what you would have if they more accurately ascertained talc use.
Q. But for that they would have been higher. Is that what you are saying?
A. Yes.
Q. When I said, misclassification, would it be more correct, it is nondifferential misclassification?
A. Yes.

MS. PARFITT: Your Honor, I have no further questions.

Dr. McTiernan, thank you very much.

Your Honor, thank you for your time.

MR. WILLIAMS: Your Honor, may I have five-minutes?

THE COURT: Yes.

RECROSS-EXAMINATION
BY MR. WILLIAMS:
Q. Doctor, I'll be as brief as I can.

The first topic you were asked some questions on, the IARC 2012 monograph in redirect examination,

let me ask you about that. It is Exhibit A 70 in your book.

MR. WILLIAMS: If we would call up page 230, please.

Q. I'll direct you to page 230, the left-hand column, Section 1.6 midway down.

Do you agree that the 2012 IARC monograph -- strike that.

Do you agree with the portion of the 2012 IARC monograph that says that "talc containing asbestiform fines is a term that has been used inconsistently in the literature"?

A. Can you show me where that is here?

Q. The middle of the paragraph.

A. I see this.

Q. Do you agree with that statement or do you have no knowledge either way?

A. I don't have knowledge of that. It sounds like a toxicology question.

Q. Not your area?

A. Not my area.

Q. You did not include in your report IARC's statement that talc containing asbestiform fibers is a term that has been used inconsistently in the literature. True?

A. True.
Q. And you did not include it in your testimony a few moments ago either, that point?
A. True.
Q. Do you agree with IARC that the term "asbestiform talc" has erroneously been used for talc products that contain elongated mineral fragments that are not asbestiform?
A. I don't have knowledge of that either.
Q. No information of either way?
A. No.
Q. You would defer to people like Mr. Longo for that?
A. People with expertise.
Q. Do you agree with IARC differences in the use of the same term asbestiform must be considered when evaluating the literature on talc? That is on the same page a little farther down.
A. I have no knowledge of that either.
Q. And in neither your report nor in the testimony on redirect examination, did you mention any of those things that are also contained in the IARC 2012 monograph. Correct?
A. Correct.
Q. Next topic is Penninkilampi. You were asked

about that on redirect examination.

MR. WILLIAMS: If we could bring up page 5 of Exhibit A 109.

Q. We looked at this earlier. Table 1 on page 5 midway down.

With respect to the issue of dose-response, do you see the reported odds ratios for the total applications of talc use about halfway down?

A. Yes.

Q. There are just two categories of data there, less than 36 applications and more than that. Correct?

A. Yes.

Q. Now, a p-Trend, a p-Value, as you've testified, estimates how likely an observed trend is due to chance. Right?

A. It is a little more than that. It is how accurate you would be about saying that -- rejecting there being no trend.

Q. Actually, you wrote in your report that a p-Value estimates how likely the observed association is due to chance.

A. I know. I was just explaining further.

Q. You wrote in your report what I just said. Right?

A. I agree.
Q. There is no probability or p-Value trend in any of the data you reviewed in Penninkilampi. Is that right?
A. Correct. They used confidence intervals instead.
Q. There is no p-Value reported anywhere in the study?
A. For these data, no. They do have p-Values for heterogeneity and publication bias.
Q. With respect to Penninkilampi, which in your report you stated found a dose-response you did so even though the authors themselves did not conclude dose-response. Right?
A. I look at the data and, as I mentioned earlier, there were three methods to look at dose-response: one is look at the relative risk with confidence intervals; one is to do p-Value with the unexposed; and one is to do p-Value without the unexposed.
Q. In this data, the authors themselves did not report any p-Value at all?
A. They did not.
Q. Next topic counsel asked you on redirect examination, about a Taher meta-analysis. Do you recall that?

A. Yes.
Q. Let's take a look at Exhibit A 137.
MS. PARFITT: Your Honor, you were very gracious with me, so I do not want to be not gracious myself, but I think we are past our five minutes.
MR. WILLIAMS: Forgive me, your Honor, if I may, the Taher study was not part of Dr. McTiernan's articles originally included in her reference list. Counsel just raised it on redirect examination, and so I'm just simply trying.
MS. PARFITT: Your Honor, let me be heard on that. At the time of her deposition, we did not have her report. We did not have Health Canada. We supplemented all of that timely. So I don't think that's quite correct.
THE COURT: Either way, you've got another couple of minutes. You didn't take up all your time. We're not going to go at this at length, but keep it short, Mr. Williams. It will take us longer to argue the point than give the testimony.
BY MR. WILLIAMS:
Q. Now, the Taher study is not one of the articles you originally had on your list. Correct?
A. Correct.
Q. It was made public after your litigation report

was submitted as a matter of fact. Right?
A. Yes.
Q. You are not actually relying on the Taher studies for your opinions in this matter. Is that correct?
A. That's correct.
Q. The study contains a meta-analysis. Right?
A. Yes.
Q. And the authors calculated an overall relative risk of 1.28 for their meta-analysis. Right?
A. I don't have that table in front of me. Is it in one of these documents?
Q. Let's bring up page 29.
A. What's the document number?
Q. A 137.

There is the Section 3.4 meta-analysis. Do you see that reference there, 1.28 with a confidence interval of 1.20 to 1.37?
A. Yes.
Q. Please turn to the conclusion of the study. It is on page 50, if we could pull that out.

In the conclusion it says in that last sentence:

"Consistent with previous evaluations the IARC in 2010 and subsequent evaluations by individual

investigators, the present comprehensive evaluation of all currently available relevant data indicates that perineal exposure to talc powder is a possible cause of ovarian cancer in humans."

Do you see that?

A. Yes.

Q. That reference specifically states that it is consistent with IARC from 2010. Correct?

A. That's what it states.

Q. And the IARC definition in 2010 was, as we went through today, that chance, luck, bias, confounding factors could not be ruled out. Correct?

A. Yes. But I would note these authors didn't do a full causal analysis. They only did the meta-analysis part.

Q. Now, the full causal analysis that you are referring to today that you did --

A. Yes.

Q. -- includes the biological plausibility that we have gone through with you today. Right?

A. Yes.

Q. It includes the analysis of consistency that we have gone through with you today. Correct?

A. Yes.

Q. I take it you disagree with the conclusion of

the authors of the Taher study?
A. Yes.
Q. There are no scientific publications that were available to you during your review in connection with your opinions in this litigation that were not available to the authors of the Taher 2018 study. True?
A. I don't know when they did their work. Meta-analysis take a great deal of time. They may take a couple of years. I don't know when they did their reviews and when they did their evaluations.
Q. Last thing.

On the question of consistency, counsel asked you questions about Penninkilampi and Berge on direct. Do you recall that?
A. Yes.
Q. The Berge study specifically came to the conclusion -- and this is page 7 of Exhibit A 11:

"This analysis provided evidence of heterogeneity of results between the two groups of studies with an association generally detected in case-control studies but not in cohort studies."

That's what Berge concluded. Right?
A. Yes.
Q. That is one of the meta-analyses that you

believe was excellent. Right?

A. Yes.

MR. WILLIAMS: No further questions, your Honor.

THE COURT: We're good.

MS. PARFITT: We're good.

THE COURT: We'll end for the day. Now you are excused.

(Witness excused.)

(Proceedings adjourned.)

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I N D E X

C E R T I F I C A T E

PURSUANT TO TITLE 28, U.S.C., SECTION 753, THE FOLLOWING TRANSCRIPT IS CERTIFIED TO BE AN ACCURATE TRANSCRIPTION OF MY STENOGRAPHIC NOTES IN THE ABOVE-ENTITLED MATTER.

S/Vincent Russoniello
Vincent Russoniello, CCR
Certificate No. 675

Q